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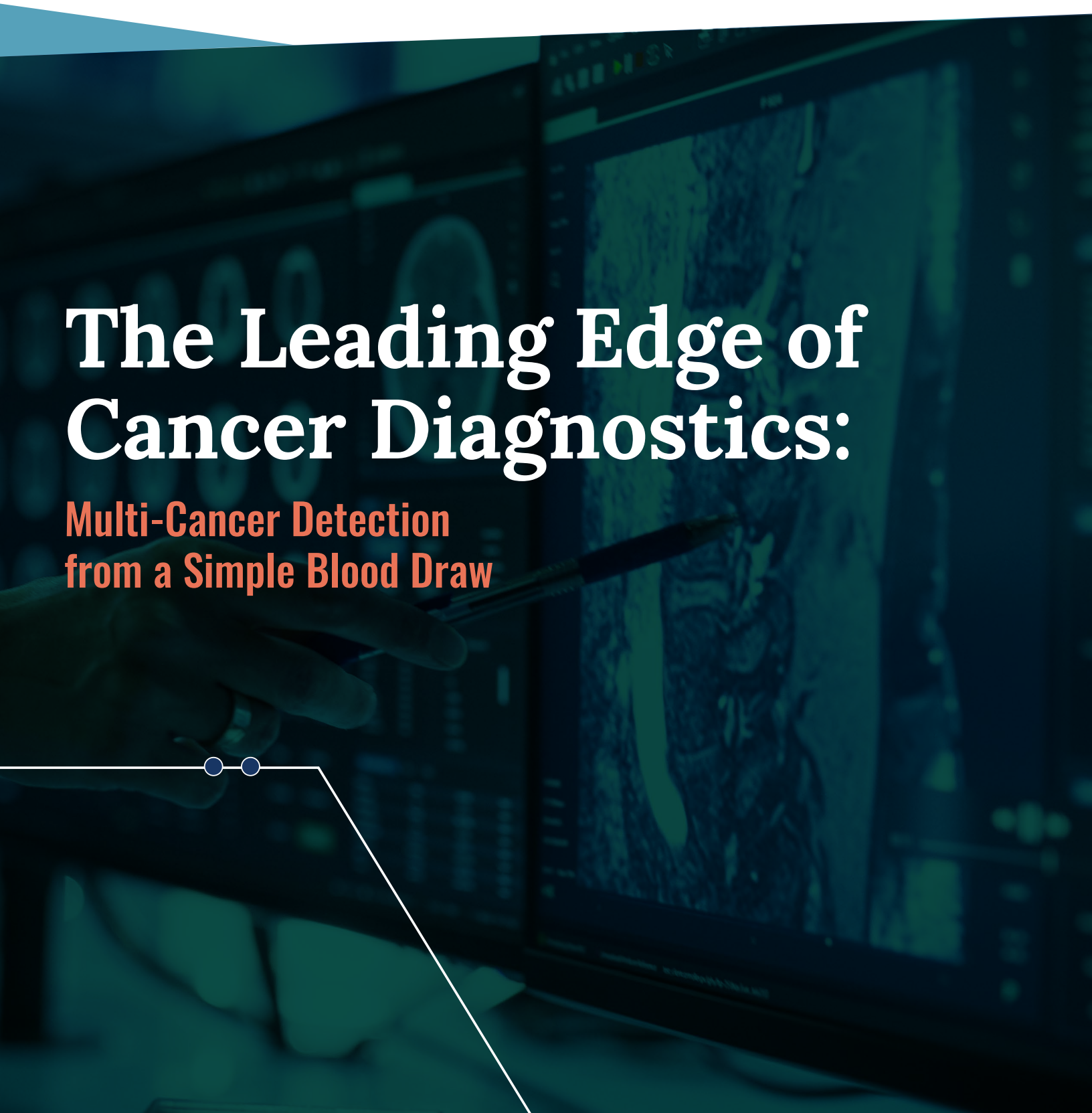


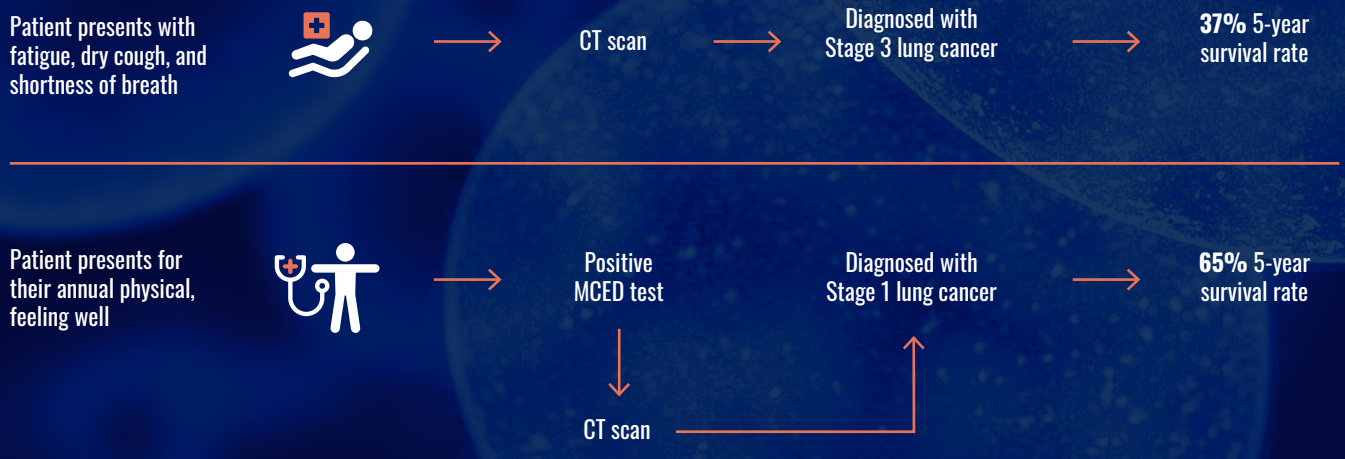
The Leading Edge of Cancer Diagnostics:

Multi-Cancer Detection from a Simple Blood Draw

Imagine if your doctor could order a test for 50 cancer types using less than four teaspoons of blood—an order of magnitude less than the blood required compared to a standard blood donation! This may sound like science fiction, but it's happening today. Though still in the early stages, the multi-cancer detection space has gone from a handful of small developers to a group of heavy-hitting biotech companies in just a few short years. The varied approaches to cancer detection, sensitivities to different cancer types, and range of stages of development within the multi-cancer detection space create a complex yet fruitful landscape of investment opportunity. Let's unpack the innovation achieved thus far, and where the field may be heading in the future.

What is multi-cancer early detection and why do we need it?

Multi-cancer early detection (MCED) tests are a novel screening method meant to simultaneously screen for 10 or more cancers with just a simple blood draw. With nearly 70% of cancer deaths resulting from a cancer type without a recommended screening,[1] MCED tests represent an urgently needed advancement in cancer screening approaches. Early detection may be key to preventing these deaths. When cancer is detected at early stages, treatment strategies are shown to be more effective, translating to improvements in survival. This is evident in cancers for which there are recommended screening approaches including breast, prostate, cervical, colorectal, and lung. In addition to the convenience aspect of MCED, an annual cancer blood test could spare patients and the healthcare system time and money spent on treatments for advanced disease that was discovered too late.



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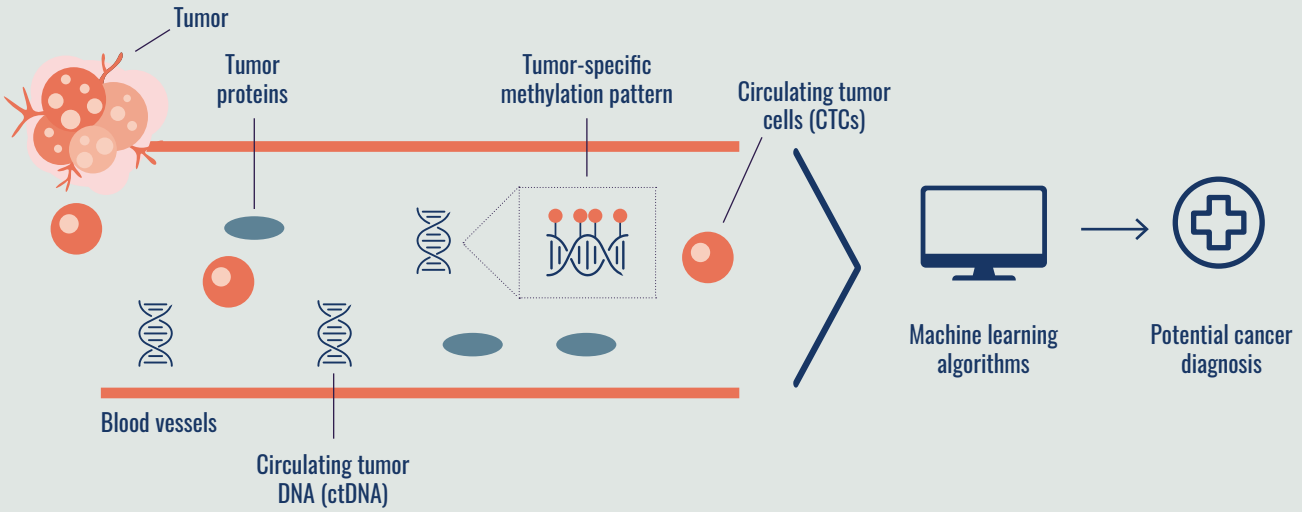
Early detection seems important, but how does it work?

It's long been known that tumor cells can shed from the primary tumor and enter the bloodstream. This is known as circulating tumor cells (CTCs), giving rise to distant metastases.[2] Additionally, tumors release cell-free DNA (cfDNA), also known as circulating-tumor DNA (ctDNA), and tumor-specific proteins into the bloodstream. ctDNA is essential in carrying the decorative marks, or biomarkers, associated with the tumor, including methylation marks or mutations.[3] MCED tests can rely on single or multiple biomarkers (i.e., methylation, mutations, proteins), with evidence from pancreatic cancer suggesting that a multi-biomarker approach may improve the test's ability to detect cancer.[4] MCED tests leverage machine learning algorithms to apply findings from clinical studies to patient samples, identifying the presence of tumor-specific biomarkers in the blood to give a cancer diagnosis. Tests can also predict the likely site of origin through unique biomarkers specific to different tissue types. Notably, all positive MCED tests today require standard-of-care diagnostics to confirm the presence of cancer because they are not yet able to confirm or refute the presence of cancer beyond a reasonable doubt. This is one area of ongoing innovation in which MCED tests can improve in the future.

MCED test performance is defined by sensitivity and specificity: Sensitivity is the ability for the test to correctly identify patients with cancer, and specificity is the ability for the test to correctly rule out those without cancer. At the present stage of development, most tests demonstrate very high specificity to limit false positives but are not incredibly sensitive, especially at early cancer stages. Advances in the use of artificial intelligence (AI) or novel biomarkers may help improve these metrics, with the goal of reaching high sensitivity and specificity, even in early-stage tumors. We are tracking updates to MCED test sensitivity data in order to identify investment opportunities as incremental improvements may change the commercial competitiveness of one test over another.



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Who are the major players in the field and how do they compare?

The most advanced MCED tests include commercially available Galleri by GRAIL and Cancerguard by Exact Sciences Corporation. While Guardant Health's Shield is approved to test for colorectal cancer, its multi-cancer version is still in development. No MCED test particularly outperforms another, with all achieving 99% specificity and a range of 50%–60% overall sensitivity (Table 1).

Though overall sensitivity—a test's ability to detect cancers across types and stages—is 50%–60% (Table 1), today's MCED tests are only able to detect early-stage cancers with 17%–35% sensitivity (Table 2). To provide perspective, while a mammogram has 87% sensitivity for stage I tumors,[8] the Galleri test is only able to identify 17% of stage I-II breast cancer.[9] This underscores that MCED tests will not eliminate the need for single cancer screening approaches until sensitivity for early-stage tumors can be improved to the levels of existing tests. Conversely, for cancers without well-established screening tools, MCED could be advantageous to patients: Galleri was able to detect stage I-II tumors with 50% or greater sensitivity for four out of five cancers accessed, that do not have recommended screening approaches.[9] This demonstrates that MCED can effectively fill an unmet need to expand early detection screening approaches to more cancer types, improving survival outcomes, alongside existing screening protocols. We are tuned in to changes in medical guidelines and prescribing volumes, aiming to correlate real-world data on uptake with improvements in test metrics to identify which tests may be preferred by doctors and patients.

Table 1

Test	Biomarker(s) Assessed	Specificity	Sensitivity	Organ of Origin
Galleri[5]	Methylation	99.5%	51.5%	88.7%
Shield[6]	Methylation, mutation, fragment	98.6%	59.7%	92.0%
Cancerguard[7]	Methylation and proteins	98.5%	50.9%	Not reported

Table 2

Company	Test	Sensitivity by stage across cancer types			
		I	II	III	IV
GRAL	Galleri[5]	17%	40%	77%	90%
GH	Shield[6]	35% (I-II)	35% (I-II)	84% (III-IV)	84% (III-IV)
EXAS	Cancerguard[7]	17%	49%	74%	87%

"Abbott recently announced an agreement to acquire Exact Sciences for approximately $21B, one of the largest health care M&A deals in the past two years. Abbott's CEO specifically highlighted Cancerguard as a cutting-edge technology within the portfolio."

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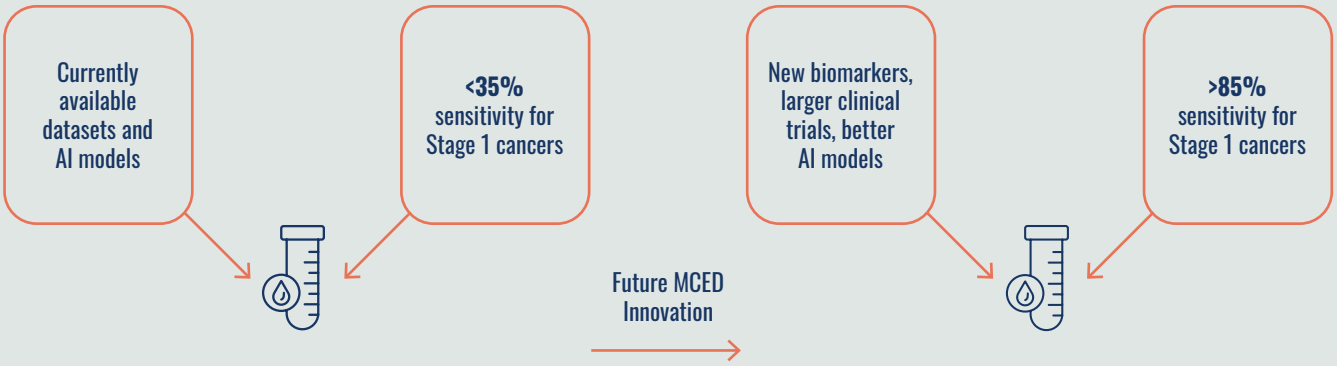

MCED is a work in progress with huge potential. What's next?

1) Better sensitivity for early-stage tumors to improve survival outcomes.

In principle, the draw of MCED testing is the ability to detect many cancers at early stages, positively impacting the survival outcome for patients. The current state of the technology does not achieve this, with up to 35% sensitivity at stage I-II cancers, and even lower in certain cancer types. Without early-stage detection, MCED screening offers limited patient benefit. With improvements in sensitivity, MCED tests are more likely to be widely adopted by physicians. Improvements in sensitivity can be reasonably achieved with the growing availability of robust datasets and rapid advancements in algorithms for detecting cancer biomarkers.

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2) Better specificity to give doctors and patients confidence in a negative result.

Currently, every positive MCED test must be confirmed through standard diagnostics. Despite high specificity for the described tests, 1% of individuals will have a false positive. If 80% of the recommended population took MCED tests, it would result in nearly 900,000 patients undergoing unnecessary diagnostic testing. Additionally, in its most recent clinical study, Grail has shown that for false positive cases, it took a median of 75 days to resolve the false positive, highlighting the burden placed on the healthcare system and potential stress experienced by the individual.[10] Studies with longer follow-up, more diverse populations, and MCED tests employing additional biomarkers may offer a strategy to improve specificity. As our knowledge grows regarding how cancer develops over time and how natural aging and lifestyle choices may affect cancer biomarkers, parameters can be further refined to ultimately improve specificity.

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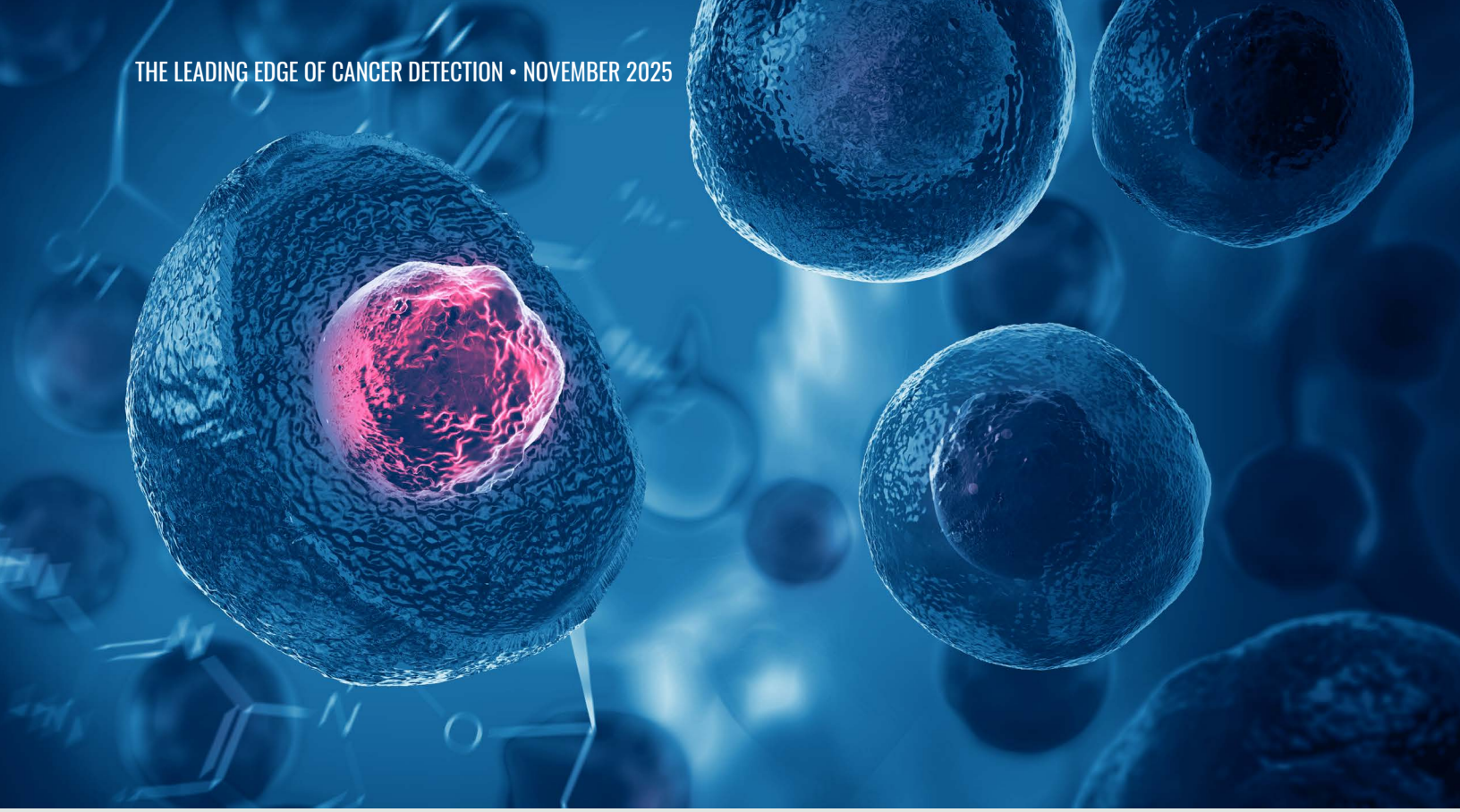

3) Positive coverage determinations for tests that expand access to more patients.

Available MCED tests carry a high price tag with sparse coverage by Medicare, Medicaid, or commercial insurance. Likewise, it's unclear how payors are handling coverage of a diagnostic follow-up resulting from a positive self-paid test. With the release of Cancerguard from Exact Sciences, the company has implemented a reimbursement system of up to $6,000 to cover diagnostic follow-up not covered by insurance, suggesting that payors may not approve tests ordered based on a positive result, limiting MCED adoption. The pending FDA submission for Galleri will open the door for FDA approval and a United States Preventive Services Task Force (USPSTF) recommendation followed by Medicare/Medicaid coverage.[11,12] This could pave the way for other tests to pursue coverage and expand access to more patients, enabling a ramp in usage.

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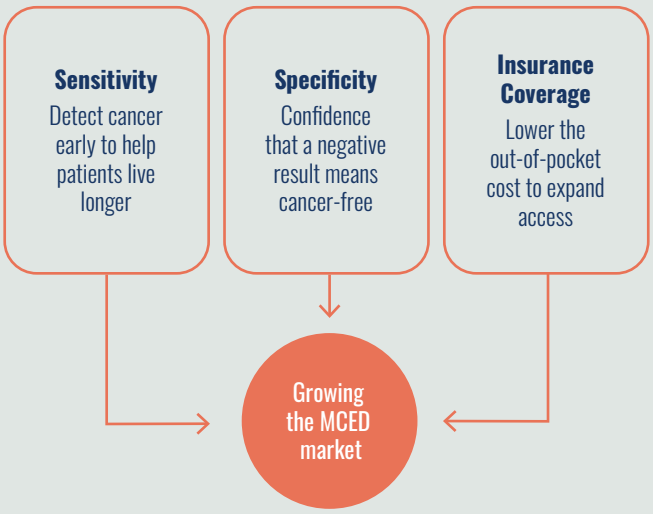

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Our approach to investing in multi-cancer early detection tools

While blood-based diagnostics have made notable advancements in the past decade, limitations in test performance for multi-cancer screening approaches preclude current widespread adoption. We believe that there are opportunities to invest in areas of innovation, specifically where AI is being used to improve test sensitivity and specificity, and where larger prospective trial designs enable real-world data to be fed into these models. We believe a combination of higher-quality data and deeper analysis could transform the MCED space into the practice-changing tool it has the potential to be.

Our aging population and the trend toward health-conscious living are driving a substantial market opportunity for multi-cancer screening approaches. Additionally, blood draws are minimally invasive and accessible across socioeconomic contexts, highlighting the potential for MCED testing to overcome barriers to cancer screening. However, without coverage for MCED tests in place, the cost is prohibitive. We look to future FDA approval of MCED tests and potential legislative changes to provide the necessary framework for payor dynamics to be improved.

At Kennedy Capital Management, we approach investment in multi-cancer early detection tools by identifying and investing in:

1

Companies that have differentiated sensitivity: As MCED developers race to implement more efficient processes using AI and better clinical data inputs, our small-cap focus enables us to evaluate and invest in companies that demonstrate differentiated sensitivity to various cancer types, which may confer a competitive advantage.

2

Companies with high-quality data inputs: Our focus on fundamental scientific research allows us to conduct a thorough analysis of clinical trial design and datasets to identify prospective trials with longer follow-up, which could improve the ability of MCED tests to detect early-stage disease.

3

Companies with the infrastructure to support, and one day commercialize, MCED broadly: A significant benefit of MCED tests is the ability to increase access to cancer screening through the ease of sample collection. We are focusing on companies that are scaling or partnering to facilitate capacity expansion.

While blood-based tests have shifted the paradigm of cancer diagnosis, limitations in today's technology make these tests fallible. We remain optimistic about opportunities in advancing AI models and ongoing clinical trials that can potentially improve test performance and transform the field of cancer diagnostics.

Important Disclosures:

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11 National Library of Medicine (NIH), June 2024, "Perspectives on Clinical Adoption Barriers to Blood-Based Multi-Cancer Early Detection Tests across Stakeholders": **https://pmc.ncbi.nlm.nih.gov/articles/PMC11204763/**

12 Prevent Cancer Foundation, 2025, "Frequently Asked Questions": **https://preventcancer.org/policy-advocacy/multi-cancer-early-detection/frequently-asked-questions**

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