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## **Early Detection for the Win: Three Stock Picks Using New Technology That Could Revolutionize the Fight Against Cancer**

**By Neal Kaufman, Portfolio Manager**

### **Key Points**

1. Cancer is the second leading cause of death globally, responsible for an estimated 9.6 million deaths in 2018, including more than 600,000 Americans.
2. Many practitioners consider early detection to be the Holy Grail in the successful treatment of cancer, and new liquid biopsy technology holds out the promise of allowing multiple types of cancer to be detected at significantly earlier stages.
3. If successful, liquid biopsy could revolutionize cancer detection and treatment. The procedure also represents a massive opportunity for investors, with a potential market of \$100 billion or more, according to market researcher Frost & Sullivan.

Cancer is the disease feared most by the majority of people.<sup>1</sup> Given its prevalence and deadliness, that fear is not without reason. It is the second leading cause of death globally, responsible for an estimated 9.6 million deaths in 2018, including more than 600,000 Americans. More than 38% of people in the U.S. are expected to be diagnosed with cancer at some point in their life.<sup>2</sup>

Barring an outright cure, many practitioners consider early detection to be the Holy Grail in the successful treatment of cancer. Liquid biopsies – diagnostic tests on liquid samples such as blood or urine rather than tissue – may just represent that Holy Grail. Liquid biopsy holds out the promise of allowing multiple types of cancer to be detected at significantly earlier stages. If successful, liquid biopsy could revolutionize cancer detection and treatment. The procedure also represents a massive opportunity for investors, with a potential market of \$100 billion or more, according to market researcher Frost & Sullivan.

A liquid biopsy is a non-invasive test that detects biomarkers, substances in blood or urine that have broken off from cancerous tumors. The two main biomarkers are circulating tumor DNA (ctDNA) and circulating tumor cells (CTCs). The more common ctDNA are small fragments of DNA, while CTCs are intact tumor cells.

With liquid biopsy, the hope is that, eventually, a simple blood test would be enough to determine if a person has cancer through the detection of biomarkers. If biomarkers are found, the DNA would then be

analyzed (sequenced) for genetic mutations that would help identify the specific type of cancer. This would allow the treating physician to match the patient with therapy that targets the mutations causing the patient's cancer.

Of course, early detection doesn't guarantee a cure, but in many cases it can dramatically improve the chance of survival. Many cancers, including some of the most common such as breast, cervical, oral, and colorectal, have a high chance of a cure if diagnosed early and treated appropriately. Early detection can also have a positive impact on the financial, societal, psychological, and emotional burden of cancer. Early stage cancer is more likely to respond to treatment and, in addition to a greater probability of survival, result in less morbidity and faster and less expensive treatment, which in turn can generate significant improvements in the lives of cancer patients and their loved ones.

In addition, liquid biopsies are quicker, easier to conduct, and far less invasive than tissue biopsies, the only other option currently available.

### *Three stocks to watch in the liquid biopsy space*

We think **Illumina, Inc. (NASDAQ:ILMN)** in which we have been invested for many years, is an interesting way to play the growth of liquid biopsy because Illumina provides DNA sequencing instruments and consumables to many of the companies developing liquid biopsies and is likely to benefit regardless of who is the winner. Illumina is also directly invested in liquid biopsies through its 2017 spin off GRAIL, which was established solely to develop liquid biopsies for early stage cancer detection. GRAIL, in which Illumina still owns a minority stake, quickly went on to raise more than \$1 billion, in what was then the largest-ever equity financing round in biopharma history.

Many companies are developing liquid biopsy tests and we anticipate several IPOs in the future. One of the first pure play liquid biopsy companies to go public is **Guardant Health, Inc. (NASDAQ:GH)**, which had its IPO in October 2018. Guardant offers a liquid biopsy test called Guardant360 for advanced cancer patients, which provides information about the mutations driving the patient's cancer and allows the treating physician to select the most effective therapy for that patient. Guardant is also developing tests for detection of cancer relapse as well as tests for early detection of asymptomatic cancer. The share price has tripled in eight months driven by revenue results that have surprised to the upside and the significant revenue opportunity if the company is successful in developing a test for early stage cancer detection. However, as a result, we think Guardant is currently quite expensive based on its price-to-sales ratio.

**Bio-Techne Corporation (NASDAQ:TECH)**, a leading developer of life sciences tools, got into the liquid biopsy business with its 2018 acquisition of Exosome Diagnostics, Inc. Exosome is developing liquid biopsy tests with a slightly different approach -- by looking at small extracellular vesicles called exosomes that are released from many cell types. The company currently has a test that determines whether men who have an ambiguous PSA result would benefit from having a prostate biopsy. The test is meant to reduce unnecessary biopsies, which are invasive and can lead to complications.

### *Drivers and risks*

A major driver of the adoption of liquid biopsies is the improved patient experience from a noninvasive approach compared to tissue biopsies, especially for patients who need a series of biopsies (to monitor and track drug-resistant cancer mutations for example). In addition, liquid biopsies only require someone trained in drawing blood, and offer a quicker turnaround time.

At this juncture, it is still very hard to detect biomarkers in early-stage cancer. Another issue is that any ctDNA found may not be from a tumor, but rather from bacteria, viruses, or even white blood cells. In addition, a product could always fail in clinical testing, or fail to get regulatory approval. Potential competition is also an issue in this increasingly crowded landscape, although the many potential applications for liquid biopsies may allow for multiple players to each develop their own niches within the market.

While there are always risks associated with any investment, we believe the opportunities in liquid biopsies are real. Baron has been a direct investor in the space since 2013, when we participated in the IPO of genomic profiling firm Foundation Medicine, Inc. at a price of \$18/share. In 2018, pharmaceutical giant **Roche Holding AG (NASDAQ:RHHBY)**, already a major investor at the time, bought the remaining shares of the company for \$137/share. We continue to actively research and find many other promising opportunities in liquid biopsy. We believe that the companies we've highlighted here are well positioned to benefit from the strong growth we foresee in this fast expanding market.

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<sup>1</sup> According to a [2015 World Health Organization \(WHO\) fact sheet](#)

<sup>2</sup> According to a [2014 World Cancer Report](#)

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Portfolio holdings as a percentage of net assets as of March 31, 2019 for securities mentioned are as follows: **Illumina, Inc.** – Baron Asset Fund (2.3%), Baron Opportunity Fund (1.3%), Baron Fifth Avenue Growth Fund (4.2%), Baron Global Advantage Fund (3.8%), Baron Health Care Fund (3.0%); **Guardant Health, Inc.** – Baron Small Cap Fund (0.7%), Baron Opportunity Fund (0.9%), Baron Global Advantage Fund (1.5%), Baron Discovery Fund (0.1%), Baron Health Care Fund (0.8%); **Bio-Techne Corporation** – Baron Asset Fund (2.1%), Baron Growth Fund (2.6%), Baron Health Care Fund (4.2%). Roche Holding AG is currently not held in any Baron portfolios.

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