A blood test for cancer

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A blood test for cancer is something of a holy grail in oncology, as it would allow cancers to be found and treated before symptoms show up, without surgery or harmful radiation.

A universal cancer test would involve the entire population being tested on a regular basis, so the commercial opportunity here is spectacular too.

Scientists have known since the 1940s that cancer cells shed tiny bits of DNA into the bloodstream (circulating tumor DNA). These fragments can be as small as 200 base pairs, and extraordinarily dilute, at less than 0.01% of the free DNA in blood.

Finding these proverbial needles is a non-trivial challenge, but it's all very possible with existing technology.

Guardant Health, our new portfolio company, is attacking this problem obliquely with a staged three-part plan – something we always love to see.

Step 1: Sequence current cancer patients – already a $200m/year business

The first part involves testing those with advanced cancers (and hence high levels of circulating tumor DNA).

Typically genetic testing a cancer involves cutting out tumor tissue and sending it to a lab. This is slow, painful, expensive and awkward: think prostate biopsies and colonoscopies.

The first line of treatment is often be started before the genetic data arrives, 3-4 weeks after biopsy.

A few years ago Guardant developed a blood test for circulating tumor DNA with a turnaround of 6 days, and there's now a convincing body of literature highlighting the test's improved speed and accuracy.

In the most common form of lung cancer (85%) Guardant's simple blood test outperformed tissue sampling in both speed and accuracy (paper), and using *both* Guardant's test and tissue sampling increased detection by 48%.

Guardant also sells tests to the next generation of biotech companies, who typically target those with particular genetic variations of advanced cancers.

This all adds up to a roaring trade: Guardant generated $200 million of 70% gross margin revenue, growing at 180% year-on-year.

Guardant has completed over 100,000 tests, and as only a small part of each blood sample is used, Guardant holds is an increasingly valuable bank of samples and data.

Step 2: Test for recurrence

The next step is to test past patients for recurrence, using the same circulating tumor DNA sequencing technology. This is an easier problem than universal screening, as the type and genetic signature is already known, but harder as the DNA is more dilute.

Circulating tumor DNA has a half-life of about 2 hours, so Guardant's test offers the possibility to track the progress of a cancer as often as required, without the issues associated with repeated surgery or radiation imaging.

In particularly well researched cancers, the specific mutations that lead to resistance are well known, and their presence can be tested in real time.

Guardant has shown they can often predict relapse well before anything shows up in an X-ray, allowing those patients to immediately restart treatment, while sparing those who don't need it.

Step 3: A universal cancer test for asymptotic individuals

The steps above have allowed Guardant to build market-leading expertise as they build towards their long-term goal.

There are three ways to test ctDNA:

1. Test the genetic code of cell-free DNA in the blood

2. Test for changes to DNA that happen (typically methyl groups that bind to DNA and switch genes on and off.)

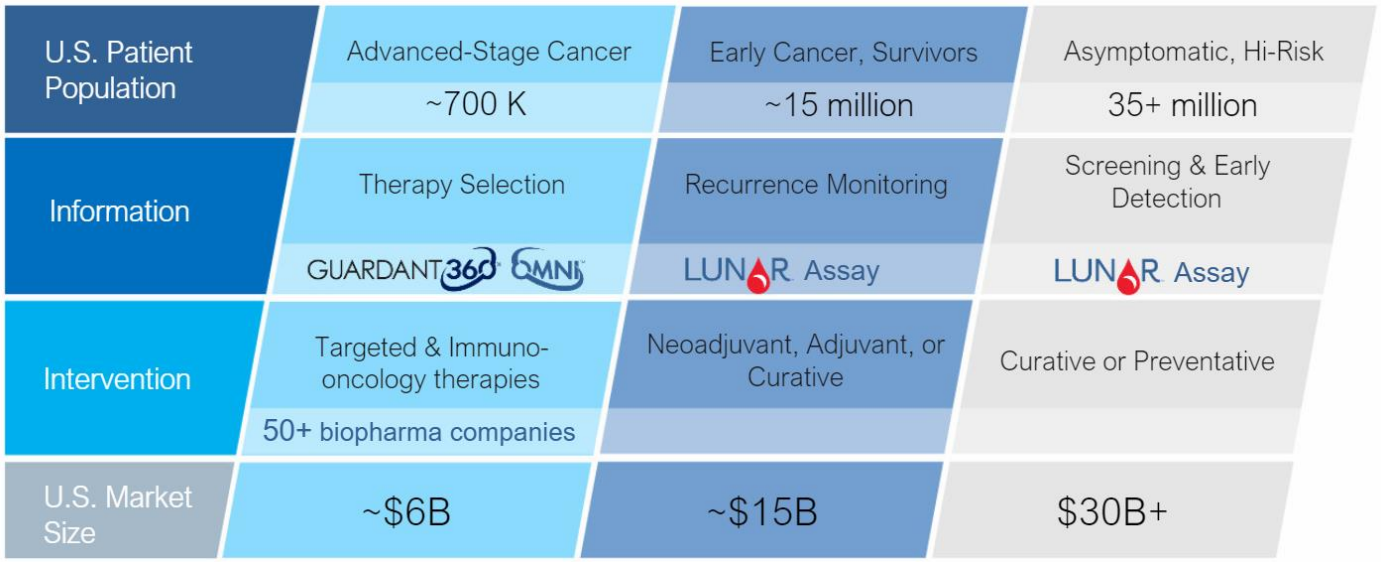
3. The fragmentation patters of DNA, as when tumor cells break down, the DNA fragments in specific ways

There are well-funded competitors in the space, but Guardant is currently unique in testing all three ways.

False positives comprise a key challenge in developing population-wide screening.

A test with 99% specificity sounds good – but if you test 100,000 people that's 1,000 false positives. In this context, those people would be subject to highly invasive regimens of unnecessary surgery and radiation, as doctors would be obliged to explore all avenues looking for a disease that's not there.

A multi-pronged approach is the best way to minimize these issues.



To summarize, Guardant is executing a clear strategy to make the following a reality:

1. Blood tests to overtake tissue biopsies when testing advanced cancer patients
2. Regular blood tests monitoring recurrence in cancer survivors
3. Testing healthy, asymptomatic people for circulating tumor DNA that indicates cancer. The current market price could be justified by (1) alone.

Guardant has sold off significantly lately, most likely because Softbank is a major shareholder. This was quite welcome, as we were able to build a position well below recent highs. Masayoshi may have actually got this one right.

We've gone quite deep on this one, so if you want to know more, please get in touch.

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