VolitionRx

Decoding the DNA of cancer

Curative therapies work best when administered early. Imagine therefore the benefits of a simple blood test that can detect cancer even before the first physical symptoms appear. Termed liquid biopsies, these tests have proved their mettle in disease monitoring and as companion diagnostics but their potential in early cancer screening remains to be unlocked. A possible roadblock is the need to enlist next-generation sequencing (NGS), to optimize sensitivity and specificity, which may make these tests, when positioned as mass-market diagnostics, too expensive, both for patients and payors. VolitionRx, a diagnostics company focused on epigenetics, is working on a solution that claims to physically isolate circulating tumor DNA (ctDNA) from background noise (no need for NGS), making for a convenient, fast and cost-effective test. Initial proof-of-concept data from a leukemia model have been encouraging, although significant clinical work is still required. Nevertheless, we see enough potential to warrant keeping an eye on the test's development pathway.

A possible breakthrough in the NGS gridlock?

Isolating tumor-derived ctDNA from otherwise healthy cell-free DNA (cfDNA) circulating in the blood has been likened to finding a 'needle in a haystack' (ctDNA makes up less than 10% of a patient's cfDNA and often less than 0.1% in early-stage cases). Available tests are generally not sophisticated enough to isolate ctDNA chemically, requiring complex, time-consuming and thereby expensive (c $1,000/test) DNA sequencing and computer algorithms (to map the entire genome to identify DNA aberrations). Volition is developing a simpler, quicker and more cost-effective solution with its first-of-its-kind liquid biopsy method using a proprietary CTCF-ChIP/qPCR method that allows for physical isolation of a class of ctDNA from cfDNA, thereby removing the need for sequencing. We discuss Volition's underlying CTCF-based approach in detail but the general theory is that CTCF (a transcription factor) binds to different sites on tumor-derived DNA versus healthy DNA, making these potential cancer biomarkers. Volition's CTCF-ChIP technology allows it to physically isolate these DNA-bound CTCF, which can then be tested for cancer using a simple polymerase chain reaction (PCR) test.

Early proof-of-concept data signal sizable potential

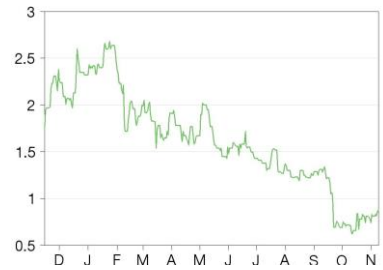
Volition has tested this new methodology using 10 quantitative PCR (qPCR) assays based on a leukemia model with good results – 74% sensitivity/96% specificity for leukemia using a 2-qPCR assay. Interestingly, some of the assays were also able to detect solid cancers (such as colorectal cancer) with high accuracy. This is despite the panels not being optimised for these cancers. More interestingly, these assays were able to spot 44% and 33% of stage I and stage II cancers, a key indicator in our opinion, supporting their pitch as effective early-stage cancer screens. We caveat that these data are preliminary and extensive clinical work is required to validate initial findings. Volition is working towards refining these tests and developing specific biomarkers for other solid cancers (CRC-specific assays are expected by Q124). Although early in its development journey, in our view the building blocks are in place for this technology to evolve as a potential disrupter in the space.

Pharma and biotech

13 November 2023

Price	**$0.74**
Market cap	**$57.8m**

Share price graph



Share details

Code	VNRX
Listing	NYSE
Shares in issue	78.1m
Net cash at end-June 2023	$16.1m

Business description

VolitionRx is a clinical diagnostics company developing easy-to-use and cost-effective blood tests for early diagnosis and monitoring of range of diseases in humans and animals including cancer and sepsis. The company's flagship Nu.Q® tests are based on the science of Nucleosomics™, which identifies and measures nucleosomes in the bloodstream or other bodily fluids, as an indicator of disease. Volition has also developed a novel cancer detection method CTCF-ChIP/qPCR for early-stage cancer screening.

Bull

- Volition's liquid biopsy test offers a simpler, faster and more convenient alternative to invasive tissue biopsies.
- By isolating ctDNA from cfDNA circulating in the bloodstream, Volition's test obviates the need for complicated and expensive NGS.
- The early cancer screening and diagnostic market remains underserved with a clear unmet need.

Bear

- The sensitivity and specificity of Volition's liquid biopsy test needs to be validated and optimized to compete with sophisticated NGS-driven tests.
- Challenges in developing and identifying the relevant biomarkers for broad-based screening of cancers.
- Further development and commercialization plans would require additional capital or securing partnering deals.

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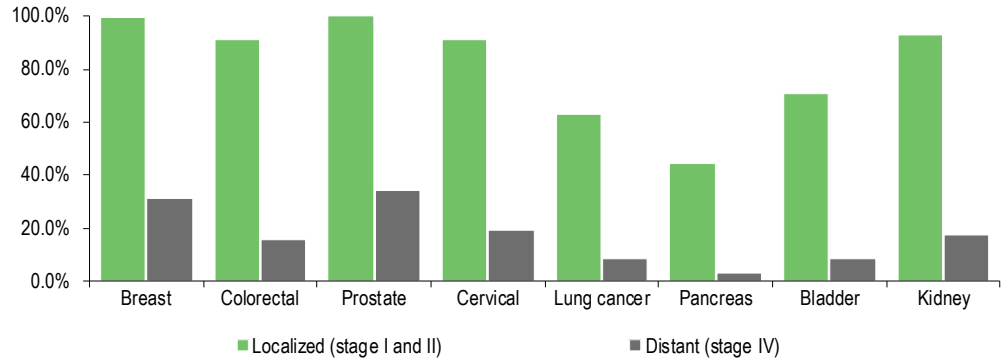
Early cancer screens in need of new blood

The growing burden of cancer and its impact on patients and healthcare systems alike needs no introduction. Cancer is the second-largest cause of mortality globally after cardiovascular diseases, accounting for one in every six deaths. In the US alone, it is estimated that over 600,000 people will succumb to cancer in 2023. According to the American Cancer Society, one in two men and one in three women will develop cancer during their lifetime.

While these figures are disheartening, advancements in medical science have meant that nine out of 10 patients live five years or longer if their cancer is detected early. Studies suggest that cancer-related deaths can come down by at least 15% if detected before metastasis/stage IV. Yet close to 50% of cancers are only diagnosed at an advanced stage (stages III and IV) and only four cancer types currently have screening tests recommended by the United States Preventive Services Task Force. These include breast cancer – mammography; lung cancer – low-dose computed tomography (CT) scans; colorectal cancer – colonoscopy; and cervical cancer – pap test/human papillomavirus testing. In addition, a fifth screening test for prostate cancer – serum prostate specific antigen testing – is available but is not openly recommended due to low specificity. In Europe, the list is even smaller with only colorectal, breast and cervical cancer having approved cancer screening programs. While these cancers represent the most common cancer types (c 50% of all cancer cases), it is also telling of the fact that an equally large population remains underserved with no recommended early cancer screening tests. Moreover, available data indicate that only 14% of cancers are currently detected through a preventative screen. This highlights the significant unmet need in this space. Exhibit 1 captures the five-year survival rates for the most common cancers, when detected early versus at a late stage.

Exhibit 1: Five-year survival rates by stages of cancer in the US



Source: SEER.cancer.gov

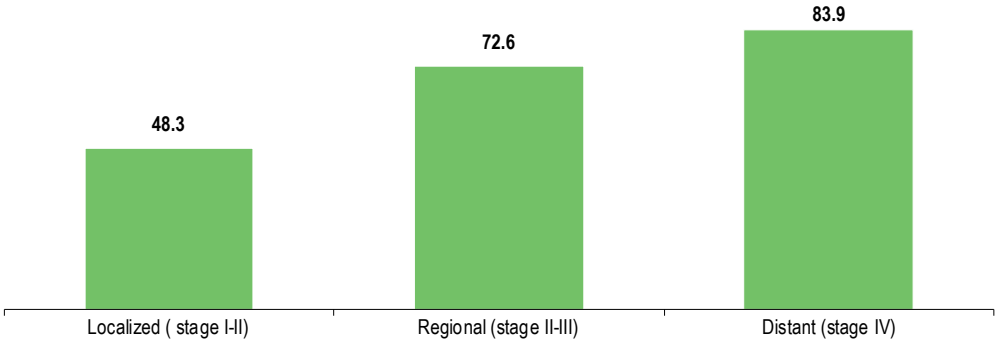
It is clear from the graphic that for most cancers, the five-year survival rates, if diagnosed early, are over 90%. An exception is pancreatic cancer where survival rates are below average as symptoms only begin showing in advanced stages (when over 80% of cases are diagnosed). An early cancer screen for pancreatic cancer would be especially beneficial if it is able to detect pre-symptomatic cases.

Even for those cancers with available screening, currently covered tests, while effective, have certain limitations (CT scans and mammography expose patients to radiation and colonoscopies are invasive, painful and inconvenient), which leads to low patient compliance rates. The appeal of a simple blood-based test to detect and analyze cancer is therefore obvious and holds promise to bridge the cancer screening gap.

Lest we forget, early cancer screening will benefit not only patients, but also the broader healthcare system given that cancer-related care is one of the largest healthcare burdens on providers today.

Early detection could mean lower hospitalization and treatment costs as well as reduced outpatients visits and emergency admissions. Exhibit 2 presents the average per patient cancer costs in the US by stage of diagnosis. It is clear from the graphic that costs rise significantly with advancing stages of cancer diagnosis, with costs at stage IV (metastasis) nearly double those at stages I and II (local).

Exhibit 2: Per patient cancer costs with stage of diagnosis (in $000s)



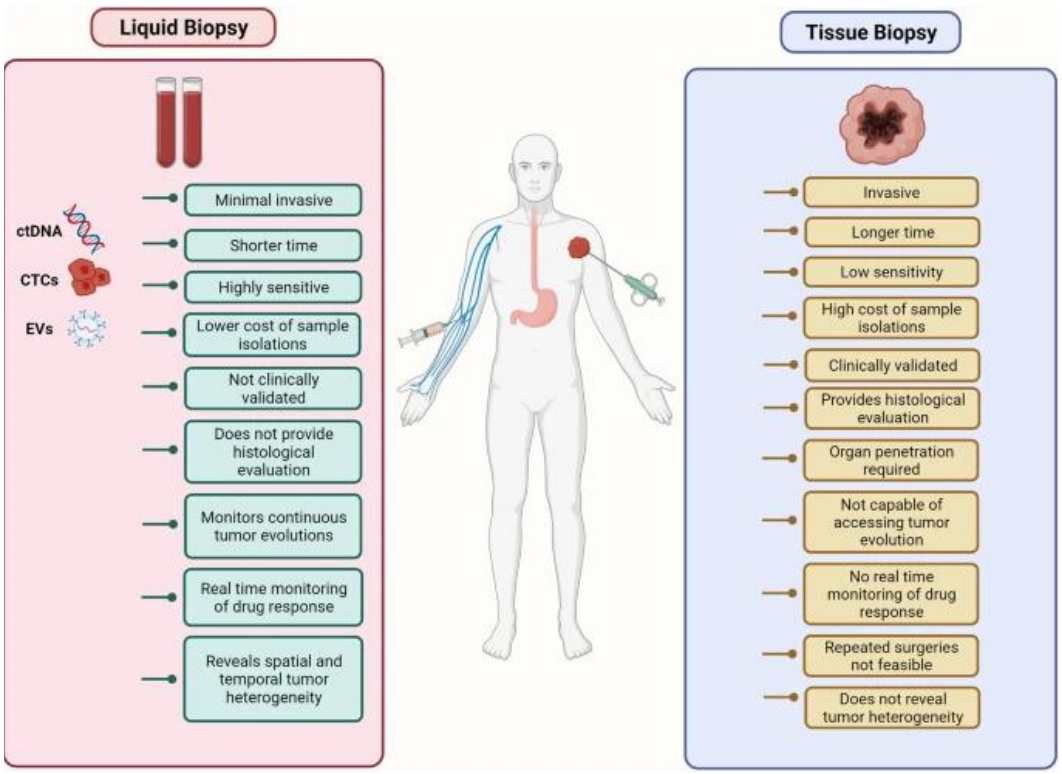
Source: Adapted from Connal, S., Cameron, J.M., Sala, A. et al. Liquid biopsies: The future of cancer early detection. *J Transl Med* 21, 118 (2023) CC BY 4.0 Deed

Liquid biopsies – a validated solution?

At its most fundamental level, liquid biopsy means the diagnosis and molecular analysis of cellular debris floating in biological fluids such as blood, cerebral spinal fluid, urine and saliva. In the case of cancer, since blood stays in contact with most tumors, liquid biopsies involve blood sampling aimed at isolating and analyzing tumor-derived entities such as circulating tumor cells (CTCs), ctDNA and tumor extracellular vesicles (EVs), which are shed into the blood stream following tumor apoptosis, necrosis or active excretion. These entities reflect the molecular characterization of the underlying tumor (such as DNA mutations) and therefore analysis of their genomic data should present insights on the presence and type of cancer. Of these, the ctDNA-based approach has garnered particular attention in the scientific community as an effective biomarker for cancer diagnosis. Cancer patients often have an elevated level of cfDNA in their serum or plasma and the proportion of cfDNA that arises from tumor cells comprises the ctDNA. Not surprisingly, much of the recent clinical activity in this space is focused on ctDNA.

Given that liquid biopsies require only a simple blood draw, they are a less invasive alternative to other types of biopsies, such as incisional, excisional or needle aspiration biopsies, which are the current gold standard of cancer diagnosis. Besides being invasive, tissue biopsies can have certain other disadvantages such as difficulty accessing the site of the tumor in certain cancers (for instance c 25% of lung cancer biopsies are unable to obtain enough tumor tissue for assessment) and challenges with tumor heterogeneity. In metastatic disease, multiple tissue biopsies may be required, which makes this exercise inconvenient and fairly painful. Exhibit 3 shows the potential advantages of using liquid biopsies over the traditional tissue biopsies. We caveat that while liquid biopsies do offer certain distinct benefits, they are currently too early in their development journey to unseat tissue biopsies for full diagnostics, and hence are most likely to be positioned as a complement rather than a replacement, One of the key reasons for this is that expected genetic alterations that signal the presence of cancer are present in much lower concentration in blood samples than tumor-derived tissue samples. As highlighted previously, ctDNA makes up less than 10% of cfDNA circulating in the bloodstream and in early-stage, pre-symptomatic cases, this ratio can be as low as 0.1%.

Exhibit 3: Advantages of liquid biopsy versus traditional tissue biopsy



Source: Lone, S.N., Nisar, S., Masoodi, T. et al. Liquid biopsy: A step closer to transform diagnosis, prognosis and future of cancer treatments. *Mol Cancer* 21, 79 (2022) CC BY 4.0 Deed

A rapidly evolving market

Liquid biopsies were first introduced as a new diagnostic concept only in 2010 and therefore are a fairly new testing paradigm in the context of medical discovery and application. The initial area of interest for liquid biopsies was their utility as diagnostics tests for tumor profiling and therapy selection in more advanced stage diseases, or 'companion diagnostics' as we commonly know them. By analyzing the ctDNA for genomic alterations, these tests are designed to predict the best therapies for the given gene aberration or mutation. Multiple liquid biopsy-based companion diagnostics have been co-developed alongside cancer drugs to assess the safety and efficacy of the specific drugs on individual patients.

The first liquid biopsy to receive clearance from the US FDA was Roche's cobas EGFR Mutation Test v2 (in June 2016) as a companion diagnostic for the company's non-small-cell lung cancer (NSCLC) therapy, Tarceva, for patients carrying the epidermal growth factor receptor (EGFR) gene mutation (10–20% of all NSCLC cases). In 2020, another two liquid biopsy tests were cleared by the US FDA as companion diagnostics: Guardant360 and Roche's FoundationOne Liquid, for several targeted therapies across solid cancers.

Another area where liquid biopsies have been gaining ground is the detection of minimal residual disease (MRD)/post-surgical recurrence, which is essentially the detection of remaining tumor cells (below the threshold of detection when using conventional methods such as CT, MRI and PET scans) following the administration of initial therapy or risk of disease relapse. Since these blood-based tests are non-invasive and easy to administer (multiple periodic tests are required during the monitoring phase), there is potential for significant market uptake. There are currently five MRD-focused liquid biopsies available in the market, of which Guardant Health's Reveal, Natera's Signatera and NeoGenomics' RaDar tests are currently covered by Medicare.

The latest application being assessed for liquid biopsies and one that has garnered significant interest from the market is early cancer detection, or as a broad population screen for pre-

symptomatic patients. The first mover in this category is Grail with its multi-cancer early detection (MCED) test Galleri, which was launched in the market in 2021 under the Clinical Laboratory Improvement Act regulations for lab-developed tests (LDT), which allows for these tests to be made available on prescription even before FDA clearance. Other contenders include Exact Sciences' Cancerguard, another MCED, and Guardant Health's Shield, an early screening test for colorectal cancer. Note that none of these tests have been cleared by the FDA yet. Given their early-stage development, we believe these tests are likely to be positioned as complements to standard-of-care screening, wherever available. An area where we see liquid biopsies gaining traction is their application in triaging patients, making for a more efficient and timely diagnostics process as well as reducing costs. Exhibit 4 presents an overview of the key players and their positioning in the liquid biopsy landscape.

Exhibit 4: Liquid biopsies competitive landscape (major players)

Company	Liquid biopsy test	Tumor type	FDA clearance	List price/test	Insurance coverage	Tech	Notes
Companion diagnostics							
Guardant Health	Guardant 360	Pan-cancer	Yes (2020)	$6,800	Yes	NGS	Approved as companion diagnostic for drugs Tagrisso, Rybrevant, Enhertu, Lumakras and Orserdu.
Roche/Foundation Medicine	Foundation One Liquid	Pan-cancer	Yes (2020)	$5,800	Yes	NGS	Bought by Roche in 2015. Approved as companion diagnostic for several targeted therapies such as Lynparza, Barftovi, Piqray and Exkivity.
MRD							
Guardant Health	Reveal	CRC, breast and lung cancers	Launched as LDT in 2021	$3,600	Yes	NGS	91% sensitivity in detecting ctDNA MRD in CRC.
Natera	Signatera	Multi-cancer	Launched as LDT in 2017	$3,920	Yes	NGS	In October 2023, Natera submitted first module of its PMA application for Signatera as companion diagnostic in muscle-invasive bladder cancer.
NeoGenomics/Inivata	RaDar	Multi-cancer	Launched as LDT in 2023	N/A	Yes	NGS	Can monitor up to 48 tumor-specific mutations. Available for breast, CRC, lung and head and neck cancer.
Cancer screening							
Grail	Galleri	Multi-cancer	Launched as LDT in 2021	$949	Private	NGS	Claims to detect over 50 cancers from one blood sample. Overall sensitivity of 51.5% and specificity of 99.5%. Average sensitivity was 16.8% for stage I disease but upwards of 90% for stage IV.
Guardant Health	Shield	CRC	Launched as LDT in 2022	$895	No	NGS	Data from the Eclipse pivotal study (released in 2022) reported test sensitivity of 83% and specificity of 90%, slightly lower than Exact Sciences' Fecal Immunochemical Test (FIT) Cologuard, which has a sensitivity and specificity of 92% and 87%.
Exact Sciences	Cancerguard	Multi-cancer	No	N/A	N/A	NGS	Developing an MCED test based on its previous CancerSeek test, which reported an average sensitivity of 61% and specificity of 98.2%. Sensitivity was 31.4% for stage I cancer. The new test aims to detect around 15 cancers from one blood draw.
Freenome	Freenome	CRC	No	N/A	N/A	NGS	A multiomics platform for early cancer detection in CRC and prostate cancer. PREEMPT clinical study ongoing in CRC.
Epigenomics	Epi proColon	CRC	Yes	N/A	No	PCR	In January 2021, the CMS rejected Medicare coverage of the Epi proColon test as it did not meet the condition of sensitivity and specificity of at least 74% and 90%, respectively. The test was discontinued in 2023 after the company failed to raise funds for a pivotal trial of the next-generation version of the test. In October 2023, Epigenomics was acquired by New Day Diagnostics for up to $12m.

Source: Evaluate Pharma, Edison Investment Research. Note: Both PCR and NGS are molecular diagnostic used for DNA testing but while PCR can only detect known sequences (comparing the DNA sample with a panel of biomarkers), NGS can profile the whole genome to detect both known and novel genetic modifications. NGS, however, is significantly more complex, time-consuming and expensive versus PCR.

But staking claim as early cancer screen comes with challenges

To be able to stake a claim as a valid alternative or even as a complement to tissue biopsies, these blood-based tests need to deliver a high degree of sensitivity (accurately identifying patients with cancer with low false negative instances) and specificity (accurately eliminating participants who do not have cancer with low false positive cases). However, this is challenging because of the low levels of circulating ctDNA in the blood. Moreover, the structure of ctDNA and healthy cfDNA from a person is nearly identical, making isolation even more difficult. In fact, it is currently not possible, to our knowledge, to separate ctDNA from cfDNA chemically and therefore accurate analysis of and inferences from aberrations in DNA (such as methylation of mutations) requires extensive DNA sequencing followed by complex computer bioinformatics to interpret findings. Current liquid biopsy workflows include taking blood samples, separating the DNA fragments from the plasma, extracting and amplifying the DNA, library preparation, followed by NGS and bioinformatics (Exhibit 5).

Exhibit 5: Current ctDNA liquid biopsy workflow

Source: adapted from Volition webinar presentation, October 2023

Given the complexities and expertise required with NGS, the costs of these tests are expectedly high (the Grail and Guardant early cancer screens are priced at $949/test and $895/test, respectively), which, when seen in the context of these tests being pitched as cancer screens for a large population of asymptomatic albeit high-risk patients, will quickly add up to sizeable total costs for both payors and individuals, if not covered. The turnaround time for these tests is fairly long too, taking up to two weeks to deliver results. These factors could act as deterrents to the uptake of these liquid biopsies as cancer screening tools. A relatively inexpensive and simple alternative that could easily be incorporated as part of standard cancer screening could therefore be better suited to fill this demand gap, provided that satisfactory sensitivity and specificity criteria are met.

The Volition vantage

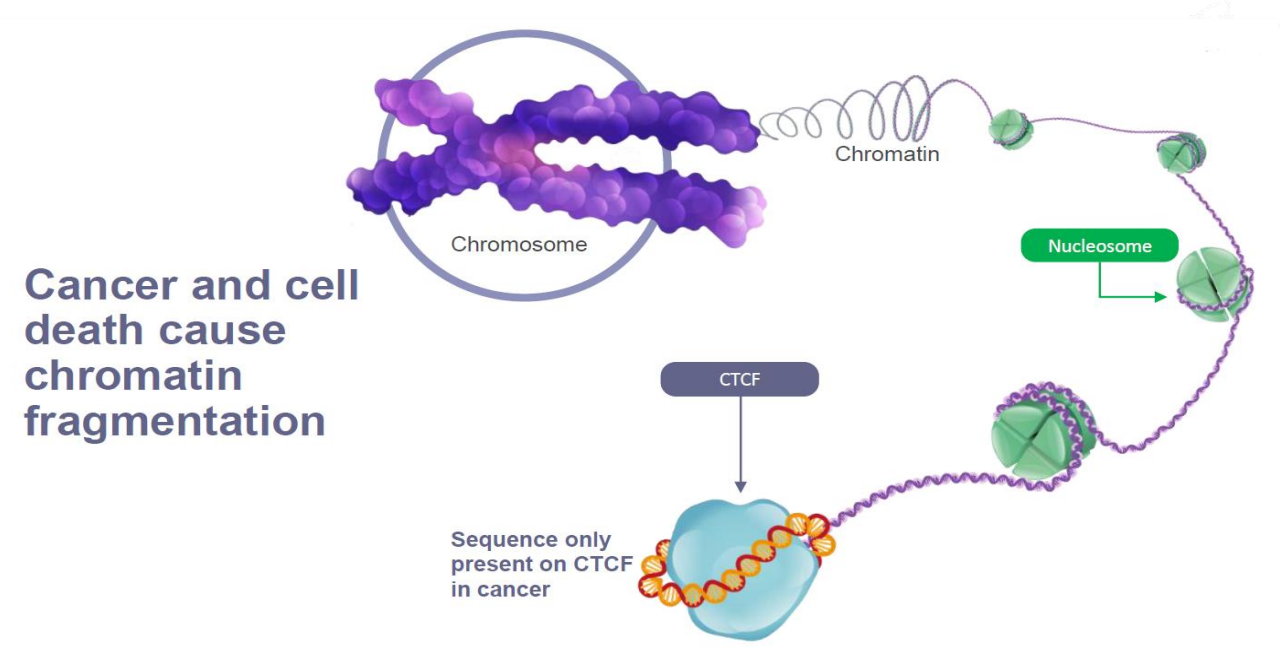
VolitionRx, a diagnostics company focused on epigenetics, is working on developing a first-of-its-kind, novel cancer detection method that allows for physical separation of ctDNA from cfDNA using a proprietary CCCTC-binding factor-chromatin immunoprecipitation (CTCF-ChIP) method, which can then be analyzed using a simple PCR test. This appears to be a faster and more cost-effective diagnostic method versus NGS.

Although the science behind this methodology and test is complex, we try to present it succinctly to provide a background and illustrate how it is differentiated from what is already available in the market.

Cell-free DNA, the core focus of liquid biopsies, circulates in the bloodstream in the form of fragments of protein-DNA complexes. Most of these protein-DNA complexes are nucleosomes (negatively charged DNA strands bind with positively charged proteins called histones to form nucleosomes, which then string and fold together to form chromatin). However, there are several other such protein-DNA complexes, including CTCF, which is a transcription factor/protein that also binds to DNA and is responsible for maintaining and regulating the architectural integrity and 3D structure of chromatin (CTCF binds together strands of DNA forming chromatin loops, and anchors

DNA to cellular structures). Exhibit 6 presents a schematic of chromatin's components and structure.

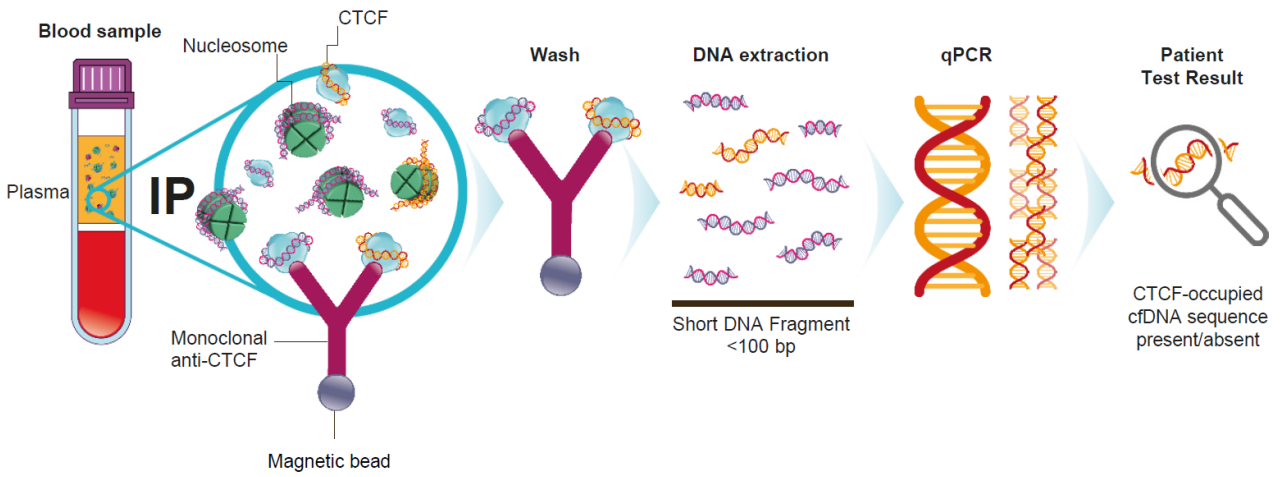
Exhibit 6: The structure of chromatin



Source: Volition webinar presentation, October 2023

CTCF binds to over 60,000 sites in the human genome, of which c 5,000 are highly conserved between different tissues and species. In the case of cancer, these binding sites may change – there may be loss of occupancy in some cases and but also gain of occupancy in other cases. Volition asserts that the DNA sequences with gain of occupancy are therefore biomarkers for cancer as they do not occur in the CTCF of a healthy person. Using the occupancy properties of CTCF, cancer-specific DNA sequences can then be isolated. Volition has developed a wet chemistry pathway that it indicates is able to identify and physically isolate tumor-derived chromatin fragments from background DNA of the same sequence, using ChIP, which utilizes an anti-CTCF monoclonal antibody to pull out all the DNA-bound CTCF from the plasma. Following this, DNA is separated from the antibody, which can then be tested using a simple PCR test designed to confirm the presence of cancer (Exhibit 7).

Exhibit 7: Volition's CTCF-ChIP/qPCR test mechanics



Source: Volition webinar presentation, October 2023

Volition tested this new method in a small clinical experiment (consisting of samples from cancer patients, as well as patients with inflammatory conditions and healthy volunteers) and was able to identify 29 CTCF gain of occupancy binding site sequence biomarkers. The company developed qPCR assays for 10 of these biomarkers, all based on a leukemia model.

Clinical proof-of-concept promising, although very early stage

The 10 qPCR assays were tested on samples collected from 74 subjects with cancer – leukemia (n=31), breast (n=10), prostate (n=10), liver (n=10) and colorectal cancer (n=13) – along with 50 control subjects, including 15 subjects with an inflammatory condition. The results from these panels, as disclosed by the company, are encouraging – all assays were effective in detecting leukemia and while some biomarkers specifically pointed at leukemia, others were also able to identify different solid cancers with a fairly high degree of accuracy. From the panel data published by the company at the European Society for Medical Oncology Congress 2023, we notice that one of the qPCR assays was able to detect 61% of leukemias with a high 98% specificity, and the sensitivity rose to 74% by adding a second qPCR panel to the test (albeit at a slightly lower specificity of 96%). More interestingly, these panels were able to detect solid cancers as well as early-stage cancers, with fairly high sensitivity: a 2-qPCR assay was able to detect 77% CRC cases at a 92% specificity. To provide context, Exact Sciences' FIT Cologuard (the current leader in the noninvasive colorectal cancer screening market) has a sensitivity and specificity of 92% and 87%, respectively, and Guardant Health's Shield liquid biopsy test for CRC has a sensitivity of 83% and specificity of 90%.

Exhibit 8 presents the sensitivity (by cancer type and stage) of another 2-qPCR assay tested by Volition for solid cancers (90% overall specificity).

Exhibit 8: Sensitivity data from a 2-qPCR assay

Solid cancers	patients	positive	sensitivity
• CRC	13	9	69%
• Breast	10	5	50%
• Prostate	10	5	50%
• Liver	10	6	60%
TOTAL	**43**	**25**	**58%**

Solid cancers	patients	positive	sensitivity
• Stage I	9	4	44%
• Stage II	9	3	33%
• Stage III	9	6	67%
• Stage IV	16	12	75%
TOTAL	**43**	**25**	**58%**

Source: Volition webinar presentation, October 2023

The sensitivity figures for solid cancers are indeed encouraging given that these assays were not optimized for these cancers. Volition is now working on identifying and developing individual biomarkers, specific to each cancer, which could possibly improve the accuracy of the test even further. The initial focus will be on CRC, followed by tests for lung, breast, prostate and liver cancers, which could possibly be combined to create a multi-cancer testing panel. Management is estimating a Q124 timeline for developing biomarkers specific to each cancer and presenting proof-of-concept data for these individual cancers throughout 2024.

Importantly, this panel was able to spot 44% and 33% of stage I and stage II cancers, a key consideration given the focus on effective early-stage cancer screening. In contrast, Grail's MCED test Galleri, currently available in the market, reported a 16.8% sensitivity for stage I disease and 40.4% for stage II disease.

While these results provide proof-of-concept for Volition's novel liquid biopsy test, we maintain that the data presented are very preliminary and need to be validated through significantly larger clinical studies. While test accuracy (both sensitivity and specificity) will continue to be the primary driver of market acceptance and commercial uptake, we believe that given the health economics of a population-wide screening test, the lower expected price of Volition's liquid biopsy test (c $100/test vs c $1,000 charged by other available tests) could tilt the scale in its favor should these early results persist and possibly improve over larger trials.

Sizeable commercial opportunity

Given the growing utility of liquid biopsies across the cancer management continuum, the prospects of these tests remain strong. The global addressable market is estimated to be $70–100bn, highlighting the sizeable potential. Within the early cancer screening subset, although the market is fairly nascent, more than 20 tests are currently believed to be in various stages of development. The commercial and business potential of any promising treatment under development is significant, as highlighted by the spate of M&A and licensing deals in the liquid biopsy space in recent years. Exhibit 9 presents some of the major deals in the space.

Exhibit 9: Selected liquid biopsy deals

Target	Acquirer	Acquisition date	Focus area	Acquisition price
Haystack Oncology	Quest Diagnostics	April 2023	MRD	$450m including $300m upfront payment and up to $150m in additional milestone payments
Thrive	Exact Sciences	October 2020	Early cancer detection	$2.15bn including $1.7bn upfront payment and up to $450m in additional milestone payments
ArcherDx	Invitae	October 2020	MRD	Upfront payment of $325m and $561m in stock (30m Invitae shares at $18.71/share). Additional payment in the form of 27m Invitae shares on achievement of certain milestones.
Grail	Illumina	September 2020	Early cancer detection	$8bn ($3.5bn cash and $4.5bn in stock). The acquisition is under anti-trust investigation.
Foundation Medicine	Roche	June 2018	Companion diagnostic	$2.4bn to acquire the remaining 44% stake in the company. 56% stake had been acquired by Roche in 2015 for $1bn.

Source: Evaluate Pharma, Edison Investment Research

Summary

The health burden of cancer continues to grow, demanding constant innovation and improvement in both diagnosis and treatment. Over the past decade, liquid biopsies have grown in prominence and their clinical applicability has expanded, courtesy of their simplicity, convenience and improving accuracy. These approaches are now relatively well developed for cancer therapy monitoring (companion diagnostics) and disease relapse (MRD), but also hold incredible potential, in our view, in the cancer early detection and screening field, an area that still remains untapped. Screening broad populations comes with its own challenges, with accuracy (particularly the possibility of false positives) being just one. Another key consideration is likely to be pricing and given that Medicare does not usually cover tests that screen healthy people, these charges would have to be attractive enough to be acceptable as out-of-pocket expenses.

In this note we have discussed VolitionRx's experimental, first-of-its-kind liquid biopsy method, which is differentiated from the currently available and under development alternatives that rely heavily on NGS to extract results and insights. Volition's technology, in contrast, appears to be much simpler (physical extraction of ctDNA), faster (a simple PCR test with no requirement for DNA sequencing) and cost-effective (one-tenth of the cost of available tests, based on management guidance). Of course, test accuracy will be vital (particularly the sensitivity for early-stage disease) and much work is still required in translating, validating and improving data from this small experimental trial to larger clinical studies. Volition is seeking to partner with key industry players to

co-develop or out-license its technology to maximize the potential of this test in meeting the stringent requirements from an early cancer screen and reaching the masses. In our view the building blocks are in place for this test to evolve as a potential disrupter and we will be keenly watching this space for more activity.

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