VolitionRx

Nu.Q advances in lung cancer management

Despite rapid advancements in cancer treatments, effective diagnostics for early screening and disease monitoring continue to be an unmet need. This is felt acutely in lung cancer, which is the leading cause of cancer-related death worldwide, with only 20% of cases diagnosed at an early stage. VolitionRx, a diagnostics company focused on the detection of life-altering diseases, such as cancer, continues to build clinical evidence for its Nu.Q® Cancer test as a multi-pronged diagnostic tool to enhance screening, treatment selection and disease monitoring in lung cancer. By detecting circulating nucleosomes associated with tumor activity, Nu.Q Cancer offers a compelling low-cost, quick-turnaround cancer screening and monitoring alternative/complement to existing diagnostic tools, particularly complex and time-consuming biomarker-based blood tests requiring expensive next-generation sequencing (NGS).

Lung cancer diagnostics: An underserved need

While low-dose computed tomography (LDCT), the current standard for lung cancer screening, has been shown to reduce lung cancer mortality by c 20%, its adoption continues to face significant limitations, such as low uptake among eligible populations (c 16% in the US), high false-positive rates (c 20%) and restricted eligibility criteria focused mainly on heavy smokers. This results in many high-risk individuals being excluded or undiagnosed until they are in advanced stages of the disease. Furthermore, LDCT is not equipped to provide the prognostic insights needed to guide personalized treatment decisions. This highlights the pressing need for complementary diagnostic tools, particularly non-invasive, cost-effective blood tests such as Nu.Q Cancer, which can improve accuracy, expand access and support detection across a broader patient population.

Nu.Q Cancer test: An effective complement to SOC

Volition's Nu.Q Cancer test uses fragments of chromosomes (nucleosomes) released into the bloodstream following cell death as biomarkers for cancers. The Nu.Q test specifically quantifies H3K27me3, a modification of histone H3.1 believed to play a significant role in lung cancer development, metastasis, and treatment response. Unlike NGS-based molecular tests in development, Nu.Q is built on the traditional enzyme-linked immunosorbent assay (ELISA) platform and can be easily integrated into existing lab protocols at low cost. We believe this offers a distinct competitive advantage from an administrative and regulatory perspective. In this report, we discuss the most recent clinical evidence presented by VolitionRx and its collborators (based on both retrospective and prospective studies) supporting the utility of the Nu.Q Cancer test across the continuum of lung cancer management, including early screening, detecting measurable residual disease (MRD), recurrence monitoring and prognostic insights for treatment selection.

Historical financials

Year end	Revenue ($m)	PBT ($m)	EPS ($)	DPS ($)	P/E (x)	Yield (%)
12/23	0.8	(35.7)	(0.50)	0.00	N/A	N/A
12/24	1.2	(27.3)	(0.31)	0.00	N/A	N/A

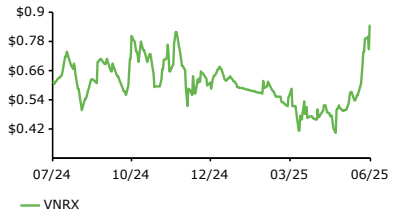
Source: LSEG Data & Analytics

Healthcare

2 July 2025

Price	**$0.77**
Market cap	**$79m**

Share price performance



Share details

Code	VNRX
Listing	NYSE
Shares in issue	103.0m
Net cash/(debt) at 31 March 2025	$(4.1)m

Business description

VolitionRx is a clinical diagnostics company developing easy-to-use and cost-effective blood tests for early diagnosis and monitoring of a range of diseases in humans and animals, including cancer and sepsis. Its flagship Nu.Q tests are based on the science of Nucleosomics, which identifies and measures nucleosomes as an indicator of disease. VolitionRx has also developed a novel enrichment method, 'Capture', to enable early-stage detection of cancer.

Bull points

- Volition's Nu.Q Cancer test offers a simpler, faster and more convenient alternative to complicated and expensive NGS-backed molecular testing.
- The Nu.Q platform is highly scalable and agnostic to legacy venues, technologies and populations.
- The early lung cancer screening and diagnostic market remains underserved with an unmet need.

Bear points

- Challenges in gaining acceptance for Nu.Q will require advocacy of KOLs to support education and integration into established protocols.
- Potential commercialisation challenges may require winning incremental partnering deals.
- Potentially slower route to market with 510(k) device application pathway.

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Edison profile page

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Early cancer diagnosis is a predictor of future survivability

Cancer remains one of the leading causes of mortality worldwide (accounting for one in every six deaths, with over 600,000 annual deaths in the US alone), with global incidence projected to rise dramatically over the coming decades. Despite significant advances in therapeutics, survival outcomes continue to hinge on a single, critical factor: early detection. When diagnosed at an early stage, many cancers, including lung, colorectal, breast and prostate cancer, can be treated with curative intent. Yet, the majority of cases are diagnosed at advanced stages, where survival is poor and treatment largely palliative. This underscores the need to expand access to effective screening and diagnostic technologies.

Within the broader oncology indications, the call for more effective early diagnostic tools has been loudest for lung cancer, the leading cause of cancer-death worldwide. Lung cancer is responsible for 20% of all cancer-related deaths, but accounts for only c 12% of new cancer diagnoses. The primary reason for this discrepancy is straightforward: most lung cancer cases are diagnosed too late. Lung cancer is typically asymptomatic in its early stages and by the time symptoms appear (such as persistent cough, chest pain or breathlessness), the disease has often progressed to Stage III or IV. This is reflected in the survival rates. According to the American Cancer Society, the five-year survival rate of early stage (localized) non-small cell lung cancer (NSCLC, c 85% of all lung cancer cases) is 65% versus less than 10% for advanced (Stage IV) cases. Yet, over 50% of lung cancer cases are only diagnosed once the cancer has metastasized. The need for better, broader and more accurate early diagnostic screening is therefore imperative.

Nu.Q offers strong potential in lung cancer detection and management

Because of lung cancer's close association with smoking, the Centers for Medicare & Medicaid Services (CMS) recommends screening using LDCT for those aged between 50 and 80 with a ≥20-pack per year smoking history and cessation less than 15 years previously. This results in 13 million people who are eligible for screening in the US. In 2022, the European Commission recommended a targeted screening program for lung cancer in Europe, although the pace of adoption has varied across nations. Early detection of disease using LDCT has been found to reduce death rates, as shown in landmark randomized studies such as the National Lung Screening Trial (NLST) and the Nederlands–Leuvens Longkanker Screenings Onderzoek (NELSON) trial. The NLST, which enrolled over 53,000 patients and followed them over a period of five to seven years, reported a 20% relative reduction in lung cancer mortality with the implementation of LDCT screening compared to subjects who received a single-view posteroanterior chest radiography (X-ray). LDCT is especially effective in finding pulmonary nodules, and the likelihood of malignancy rises with nodule size.

However, LDCT has been associated with high false-positive rates, with the US National Cancer Institute reporting that the average false-positive rate per screening round was 23.3% in NLST and 10.4% in NELSON. This relatively high rate of false-positives leads to many patients suspected of potentially having cancer being required to go through unnecessary and costly invasive diagnostic procedures such as biopsies, which can be distressing and put them at risk of infections or other complications. Moreover, LDCT is also associated with radiation exposure. According to the American Lung Association, only 16% of the eligible population was screened for lung cancer in 2022.

Given these limitations, there is a definitive need for more robust, sensitive and non-invasive tests to accurately diagnose pulmonary nodules and lung cancer. Researchers have looked for biomarkers that can be released into the bloodstream, given that tumor cells release various biomolecules such as cell-free DNA (cfDNA), circulating tumor DNA (ctDNA), exosomes, microRNAs, circular RNAs, circulating tumor cells (CTCs) and DNA-methylated fragments. Measuring these biomarkers can potentially assist in diagnosis, although sensitivity and specificity concerns remain, particularly in early-stage cancers, as small tumours may not shed enough detectable biomarkers. While cfDNA analysis using NGS equipment is being explored as an emerging minimally-invasive and data-rich tool for both the early detection and ongoing monitoring of cancer, its widespread adoption is currently limited by:

- the high costs associated with NGS and high-depth sequencing;
- technical challenges involving sample preparation, storage, processing and sequencing (given the low concentrations of cfDNA in plasma); and

- the risk of false positives, as the presence of cancer-related cfDNA mutations in healthy individuals can complicate sensitivity and specificity.

To our knowledge, while there are several blood-based tests in development for early detection of lung cancer as well as monitoring for MRD, none is FDA approved or widely adopted as yet. Nonetheless, the use of biomarkers holds promise, not only for improving screening and diagnostics, but also for the overall treatment and management of serious diseases such as lung cancer. Altogether, VolitionRx estimates that screening, prognostics and monitoring MRD in lung cancer represents a potential $4bn opportunity. Exhibit 1 presents an overview of selected blood-based diagnostic tests being developed for cancer indications, including lung cancer.

Exhibit 1: Cancer diagnosis and monitoring, selected players

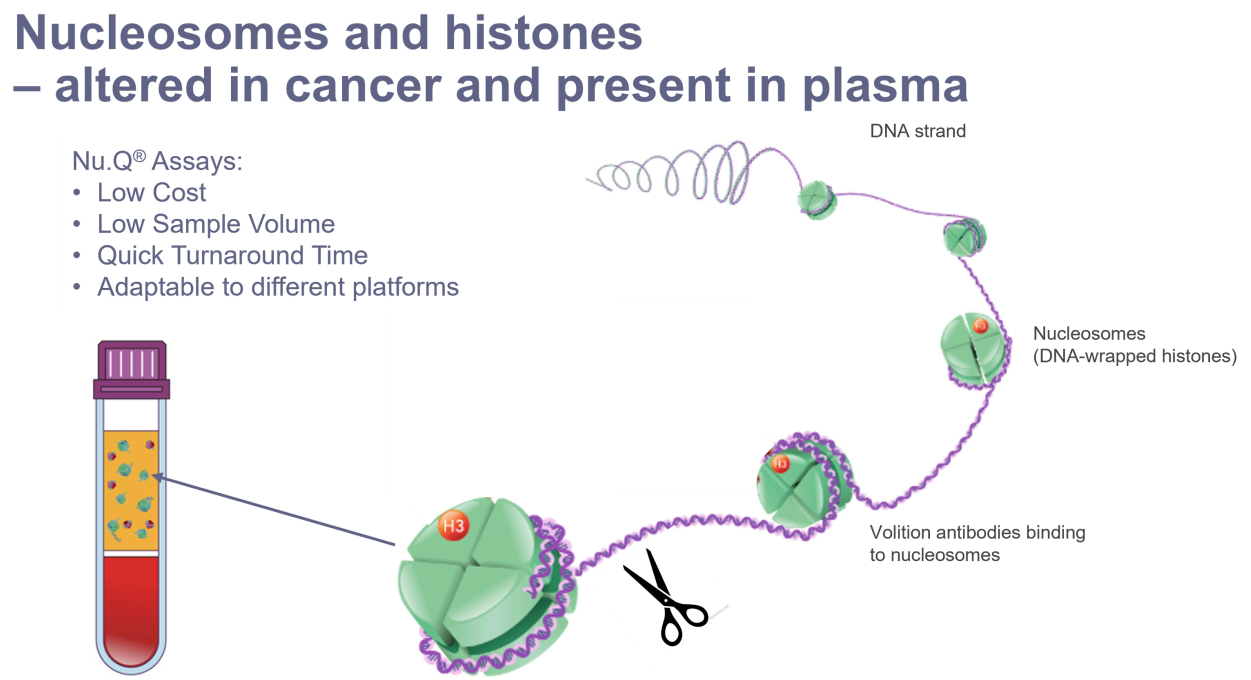
Test name	Company	Technology	Purpose	Cancer stage focus	Sensitivity	Specificity	Regulatory status
Guardant SHIELD-Lung	Guardant Health	cfDNA methylation & NGS	Early detection (screening)	Stage I–IV (focus on I–II)	Stage I–II: ~87% Stage III–IV: ~93%	~90–98.6%	Ongoing clinical trials (SHIELD-Lung). Received Breakthrough Device Designation from the FDA in June 2025. Screening test for colorectal cancer approved by the FDA in July 2024.
Galleri	GRAIL (Illumina)	cfDNA methylation & NGS	Multi-cancer early detection (MCED) for over 50 cancer types (screening)	All stages (including lung)	Lung cancer: ~75% (across all stages)	~99.5%	Not FDA-approved; US/UK clinical pilots ongoing. FDA Breakthrough Designation received in 2019.
Cancerguard EX	Exact Sciences	cfDNA methylation & NGS	MCED (screening)	All stages (including lung)	~50-64% (across all cancers and stages)	~98.5%	Clinical development ongoing (ASCEND-2, DETECT-A). Launch planned for H225.
Signatera	Natera	Tumor-informed ctDNA (mPCR-NGS)	MRD detection, recurrence monitoring	Post-treatment (any stage)	~85–92% (for recurrence)	>98% PPV	Medicare-covered (MRD); not for primary detection.
Oncodetect	Exact Sciences	Tumor-informed, personalized ctDNA-based MRD	MRD detection, recurrence monitoring	Post-treatment (any stage)	~78–91%	~80–94%	Launched in April 2025.
FoundationOne Liquid CDx	Foundation Medicine	cfDNA hybrid-capture NGS	Genomic profiling (companion Dx)	Advanced/metastatic	Not applicable to detection	High analytical specificity	FDA approved for CGP and companion diagnostics.
EarlyCDT-Lung	Oncimmune (acquired by Freenome in May 2023)	Autoantibody detection	Risk stratification (nodule triage)	All stages	~41% (improves to 77% in high-risk patients)	~90%	CE-marked; NHS pilot completed.

Source: Company documents, Edison Investment Research. Note: PPV is positive predictive value.

Histones and nucleosomes in cancer

VolitionRx has extensively studied histones and nucleosomes and their potential roles in signaling disease states. The company's Nu.Q assays are specialized in examining for nucleosomes and histones present in blood plasma and believed to be altered in conditions such as sepsis and cancer. Nucleosomes are fundamental structural units of chromosomes. They consist of a segment of DNA coiled around a core of histone proteins, which themselves provide structural support for the chromosomes, and allow the long DNA molecule segments to fit within the cell's nucleus. Histones can also regulate gene expression, and modifications to their structures can alter gene expression and potentially contribute to disease pathology (Exhibit 2).

Exhibit 2: Nucleosomes and histones, key pillars in VolitionRx diagnostic technology



Source: VolitionRx Presentation, April 2025

Cancer patients have been shown to have distinct histone post-translational modifications (PTMs) in their circulating nucleosomes, indicating their potential use or presence as cancer biomarkers. These modifications include histone acetylation, methylation and phosphorylation. There is growing evidence that these various histone modifications contribute to tumor progression and metastasis through various epigenetic and translational changes.

Volition's Nu.Q assays include proprietary antibodies that bind to specific histones taken from a blood sample and therefore can be used to identify and help quantify certain nucleosome forms, including those that are indicative of pathology, as discussed below.

Nu.Q assays offer low-cost convenience and quick turnaround times

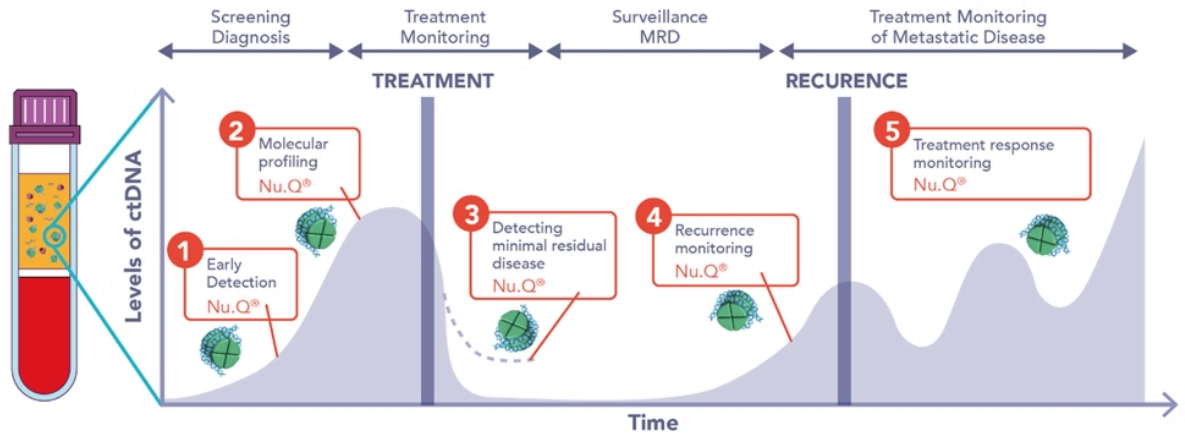
The company's Nu.Q assay tests can be offered following simple, routine blood testing, making the Nu.Q tests non-invasive and accessible to patients and hospital workflows. Nu.Q is designed to be a low-cost immunoassay that provides a quick turnaround time and, as such, can be applied and implemented in high-volume and routine clinical practice, as well as across multiple platforms and workflows (such as reference laboratories, specialist labs or point of care settings). The Nu.Q measurement process is quick and automatable, in contrast to DNA analysis, which requires additional preparation and sequencing or polymerase chain reaction (PCR), resulting in a much more time- and resource-consuming process.

Recent data confirm significance of Nu.Q measured nucleosomes in NSCLC

VolitionRx and its study collaborators at various research institutes have undertaken several studies assessing how specific nucleosomes and histones, readily detectable through Nu.Q assays, can be used for detecting and monitoring cancer.

In its April 2025 webinar, VolitionRx discussed how data from these studies show that Nu.Q can potentially be used across three areas of lung cancer: screening/diagnosis; treatment decision-making; and the measurement of recurrence (ie to identify if a change in treatment is required).

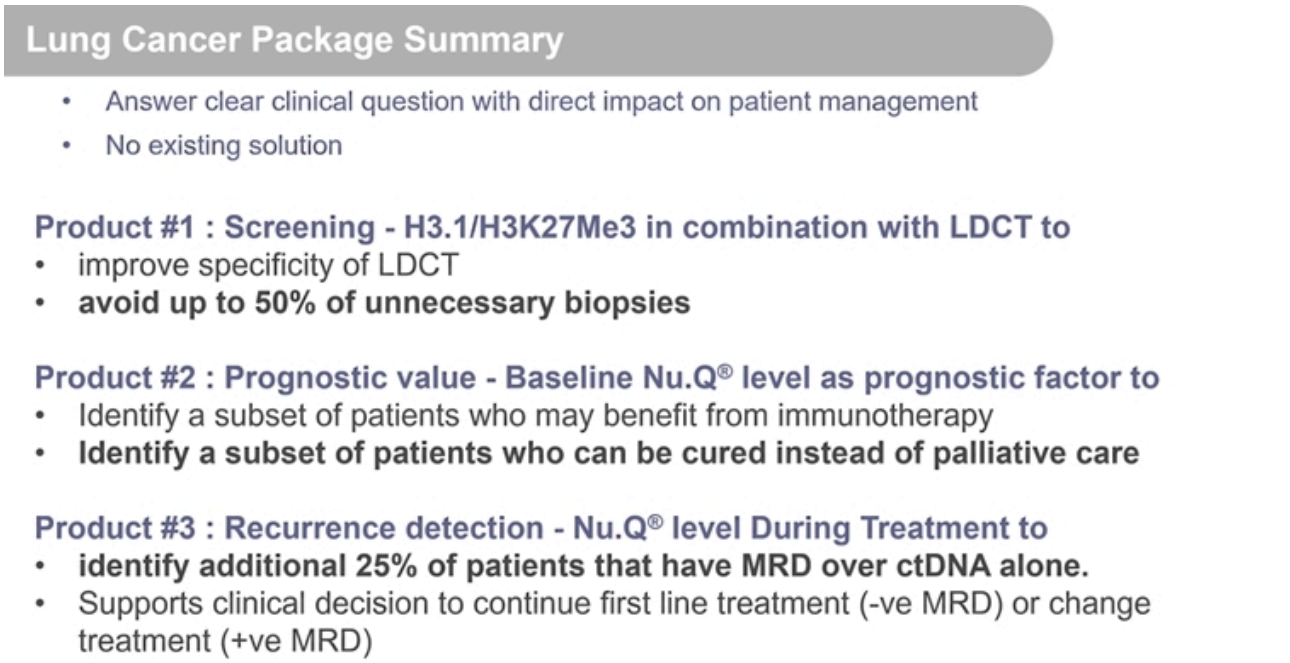
Exhibit 3: Potential applications for Nu.Q diagnostics for lung cancer detection and management



Source: VolitionRx presentation, April 2025

The company has named its assay for diagnostics Nu.Q Lung Cancer Product 1; it assesses nucleosome structures, histone H3.1 and histone H3K27Me3. In addition, VolitionRx has developed a product, called Product 2, which measures these histone levels and, as discussed below, is designed to help clinicians determine if treatment should be initiated and potentially may provide guidance on what treatment should be offered. Further, the company believes its assay technology can be used for the monitoring and detection of the recurrence of lung cancer, which may guide whether treatment should be modified during the course of therapy; the assay product for this modality is Lung Cancer Product 3.

Exhibit 4: VolitionRx's lung cancer Nu.Q product candidates



Source: VolitionRx presentation, April 2025

The clearest case for Nu.Q in lung cancer, with the strongest supportive data to date, in our view, is for screening and diagnosis, which is the aim of Product 1. In the first clinical use case (screening and diagnosis), Chen et al performed a retrospective analysis, National Taiwan University (NTU) Lung Study, between August 2019 and July 2021 of prospectively collected blood specimens from 806 patients from outpatient clinics of the National Taiwan University Hospital and the National Taiwan University Cancer Center, both teaching hospitals. Taiwan is one of the first countries to provide widespread lung cancer screening for high-risk individuals. In this study, the 806 recruited patients each had undiagnosed nodules larger than 5mm, identified in computed tomography (CT) or LDCT scans, and were classified as high risk by the attending physician.

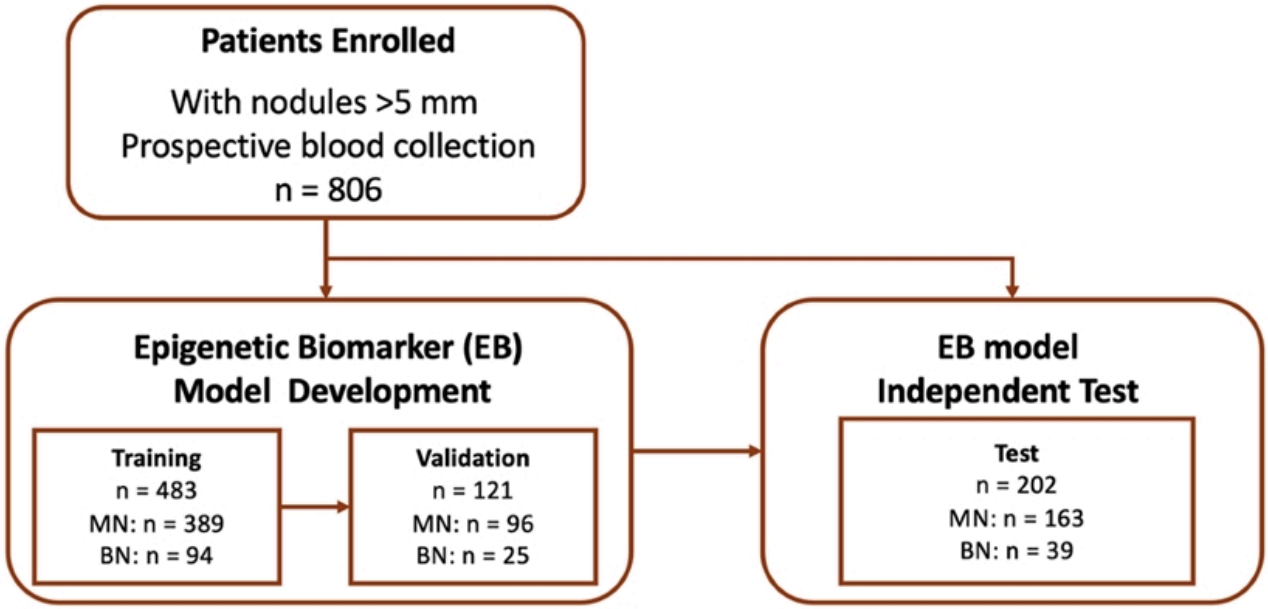
All samples were tested using Nu.Q assays, which detect specific histone structures, including H3.1 and H3K27Me3. As explained in our January 2025 note, histone H3.1 is a variant of histone protein H3, and raised levels of histones, such as histone H3.1, are an indication of the high level of cell turnover that generally occurs in cancer. H3K27Me3 is an epigenetic modification of histone H3 (reflective of a tri-methylation of amino acid lysine 27 on histone protein H3) and is also a biomarker for potential cancer, given, as stated above, that cancerous processes often lead to modifications to nucleosomes and histone structures.

NTU Lung Study shows H3.1 and H3K27Me3 improve diagnostic power

In the NTU study, researchers sought to develop an epigenetic biomarker (EB) model based on circulating nucleosomes present in the plasma, including the presence of histone variants and histone methylation, to determine if they could develop a more accurate predictive or diagnostic system or model for pulmonary nodule assessment and classification.

The study authors indicated that a predictive model should be designed to accurately identify malignant lung nodules at a sensitivity level of at least 80%, while maintaining an adequate positive predictive value (PPV, as described below) to minimize the risk of delayed diagnosis in elevated-risk populations as identified through CT/LDCT screening. To develop the model, a logistic regression approach was applied to predict benign and malignant disease states among the 806 patients recruited for the study. 75% of the patients and their study data were allocated for model development, with 80% of these patients (n=483) used for model training and 25% (n=121) for model validation. Following the completion of the model, the remaining 25% of patients and their data (n=202) were assigned to the test dataset, from which the model parameters refined from the model training and validation datasets were applied on a prospective basis to determine or predict whether subjects in this test arm had lung cancer. The accuracy of the model was then compared with the known outcomes from the datasets, which confirmed, among other findings, that the malignancy rate of the cohort (n=806) was 80.4% (158 benign, 648 malignant).

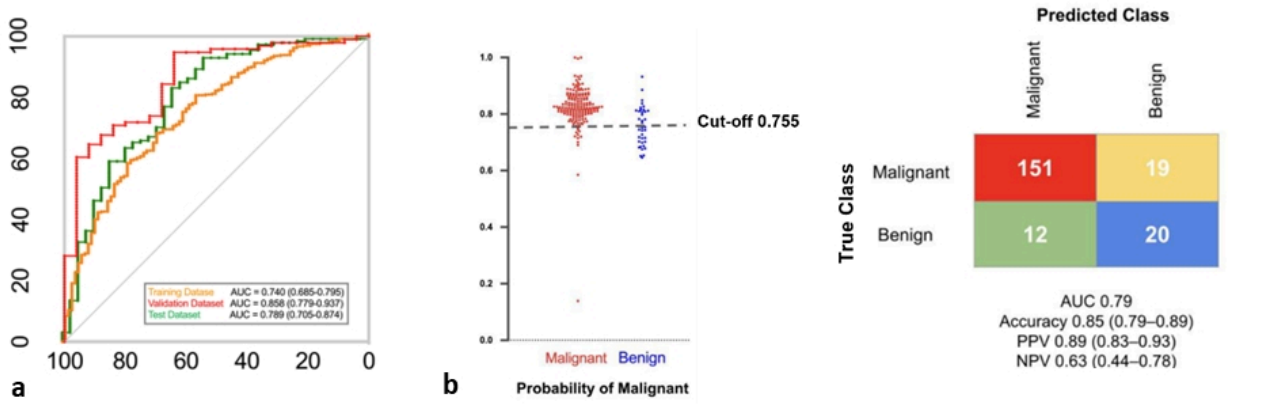
Exhibit 5: Flowchart of NTU Lung study participant enrollment and model development



Source: Chen et al. Note: MN refers to malignant nodules and BN refers to benign nodules.

During the training phase, study investigators screened multiple combinations from five quantitative epigenetic features from the blood drawn. In addition to H3.1 and H3K27Me3, they also examined epigenetic markers H3K9Ac, H3K9Me3 and H3K36Me. Ultimately, the investigators found that the accuracy of their model did not improve by adding markers beyond H3.1 and H3K27Me3. Hence, their final best-fit model only relied on these two markers (H3.1 and H3K27Me), which they determined are validated predictors of malignancy when combined with existing data (eg from the LDCT or CT screening data).

Exhibit 6: EB model determined from training and validation phases



Source: Chen et al. Note: Part (a) representative ROC curve demonstrating the classification performance of the EB model with the training, validation, and test datasets. Part (b) I shows the predicted probabilities for malignant (red) and benign (blue) nodules.

The final EB model was developed by combining data from the H3.1 and H3K27Me3 epigenetic markers (which can be extracted from a blood test) and the CT and LDCT scans. A receiver operating characteristic (ROC) curve was plotted with the model, as shown in Exhibit 6. An ROC curve is a graphical plot used to demonstrate the diagnostic performance of a binary classifier system (in this case, the presence of cancer) as its diagnostic-discrimination threshold changes (ie the test sensitivity for disease detection increases as the threshold for accepting false-positives increases). Key criteria to consider in a diagnostic test are:

- Test sensitivity: the proportion of patients with disease who are correctly identified by the test = number of true positives (TP) divided by the sum of TP plus false negatives (FN).
- Test specificity. the proportion of patients for whom the test provides a negative result (ie absence of disease) who truly do not have the disease = number of true negatives (TN) divided by the sum of TN and false positives (FP).
- Positive predictive value (PPV): the probability that a person with a positive test result actually has the disease = TP divided by sum of TP plus FP.
- Negative predictive value (NPV): the probability that a person with a negative test result truly does not have the disease = TN divided by sum of TN plus FN.

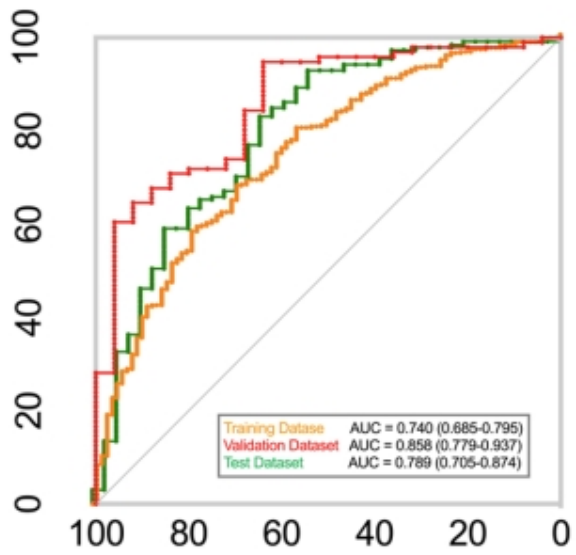
The ROC curve is formed by plotting the test sensitivity on the y-axis against the specificity on the x-axis across different threshold levels. The ROC curve illustrates the trade-off or compromise between sensitivity and specificity: as sensitivity increases, specificity decreases, and vice versa.

The closer the curve follows the left-hand axis and then the top border of the ROC space, the more accurate the test (and the more it demonstrates high sensitivity across different specificity-discrimination thresholds). A curve closer to the diagonal line (from bottom left to top right) indicates a less accurate test, as a random classifier would be expected to lie along this diagonal.

EB model outperforms established lung cancer models

The area under the curve (AUC) quantifies the overall ability of the test to discriminate between positive and negative cases, and a higher AUC reflects better overall performance and differentiation. The results from Exhibit 6 (also reflected in Exhibit 7) show an effective AUC of 0.79 from the test dataset. Using a specificity cut-off value of 0.755 (citing the desired need for >80% sensitivity mentioned by the authors) results in a PPV of 0.89 and an NPV of 0.63 in the test group. The test sensitivity was also measured at 0.93. The PPV and NPV were determined to be consistent, which the authors indicate suggests the model shows strong reliability.

Exhibit 7: EB model ROC curve

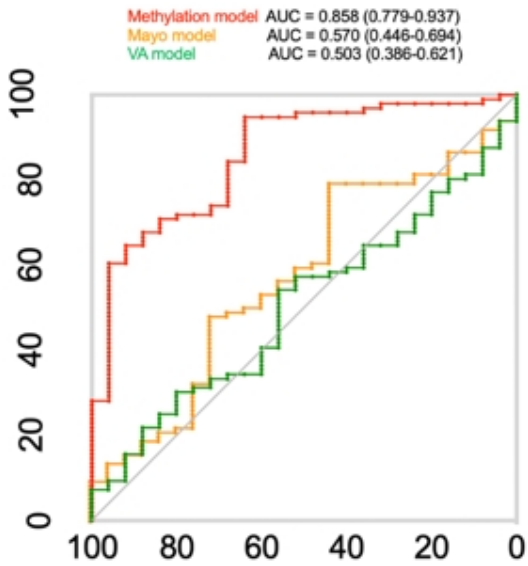


Source: Chen et al, VolitionRx

The model was also reported as showing a strong performance when limited to small lung nodules (5–10mm), with an AUC of 0.80 and a test sensitivity of 0.94. The study authors also applied the EB model to the training dataset (n=483) and the validation dataset (n=121), which provided AUC values of 0.74 and 0.86, respectively (as shown in Exhibits 6 and 7 above).

Most importantly, the study authors compared the EB model to established conventional lung cancer diagnostic models, namely the Mayo Clinic model for malignancy in pulmonary nodules (which uses three radiographic variables and three clinical variables: age, history of smoking and prior cancer history) and the Veterans Affairs (VA) model for malignancy in pulmonary nodules (which uses one radiographic variable and three clinical variables: age, smoking status and, if applicable, number of years since having stopped smoking).

Exhibit 8: EB Methylation model compared to Mayo and VA models



Source: VolitionRx

The AUC for the Mayo Model, when comparing predictions of malignancy of nodules (cancerous vs non-cancerous) compared to the true outcomes, was 0.57, versus an AUC of 0.50 for the VA model. In our view, this demonstrates the value of Volition's Nu.Q Product 1 model, as it should enable more precise and earlier detection of cancer compared to

CT/LDCT screening alone. Chen et al. report the EB model for pulmonary nodule diagnosis showed high sensitivity and accuracy with good PPVs at moderate specificity across multiple imaging characteristics, nodule types and stages of lung cancer. This would help fulfil a clear need among oncologists for a simple and reliable rapid test to help detect lung cancer and avoid unnecessary lung biopsies by over 50%.

Prospective confirmatory study underway, with data expected in Q425

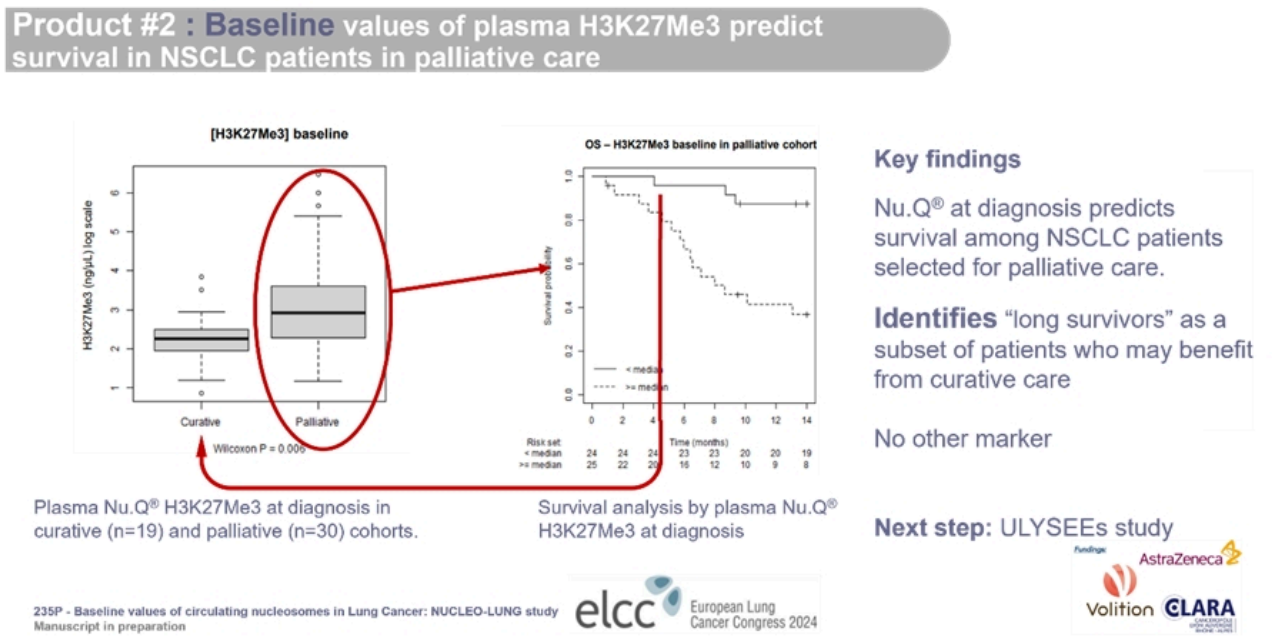
While the findings are encouraging, the development of the EB model and the NTU lung study outcomes described above were determined through a retrospective analysis of study data. The robustness of the EB model among potential commercial partners, regulators, stakeholders and eventual customers would be strengthened if the findings (for improved sensitivity and ROC-curve AUC) were confirmed in a prospectively-defined study. To this end, a prospective study, 'Epigenetic Nucleosomes in Plasma for Pulmonary Nodules Differentiation' (also called NTU V) is underway at National Taiwan University Hospital (it is a single-site study). This ongoing study is designed to recruit 500 patients, with data due in Q425. Individuals undergoing chest LDCT/CT testing will have 20mL of blood samples taken, with the plasma isolated for Nu.Q analysis. The predicted findings (presence of cancer) will be compared to the corresponding lung cancer pathology (biopsy) results. The trial aims to evaluate the diagnostic accuracy of the Nu.Q blood test for the detection of lung cancer in the Taiwanese population and compare its diagnostic performance with LDCT or CT alone. Additionally, the study will investigate the potential role of Nu.Q in lung cancer prevention and its impact on survival outcomes.

Using nucleosome data to drive treatment decisions

In addition to the demonstrated capability to improve lung cancer diagnostics, Chen et al. and VolitionRx believe that AI and data analytics can be used to integrate epigenetic-sensitive biomarkers such as H3.1 and H3K27me3 into clinical decision-making and the development of personalized treatment plans. As stated above, alterations in nucleosomes and histones can play material roles in carcinogenesis and can also be signs of cancer prognosis, progression and/or recurrence. Studies show that Volition's Nu.Q H3.1 and H3K27Me3 nucleosome detection capabilities can assist in the management of lung cancer, forming the basis for Product 2 and Product 3.

Nu.Q Product 2 is designed to determine baseline Nu.Q levels of nucleosomes such as H3.1 and H3K27Me3 and determine if this information can help tailor treatment and potentially identify those subsets of patients who, after failing earlier lines of lung cancer treatment, would benefit from additional treatment versus those who would be more suitably referred to palliative care.

Exhibit 9: NUCLEO-LUNG study shows baseline H3K27Me3 predicts survival of NSCLC patients in palliative care

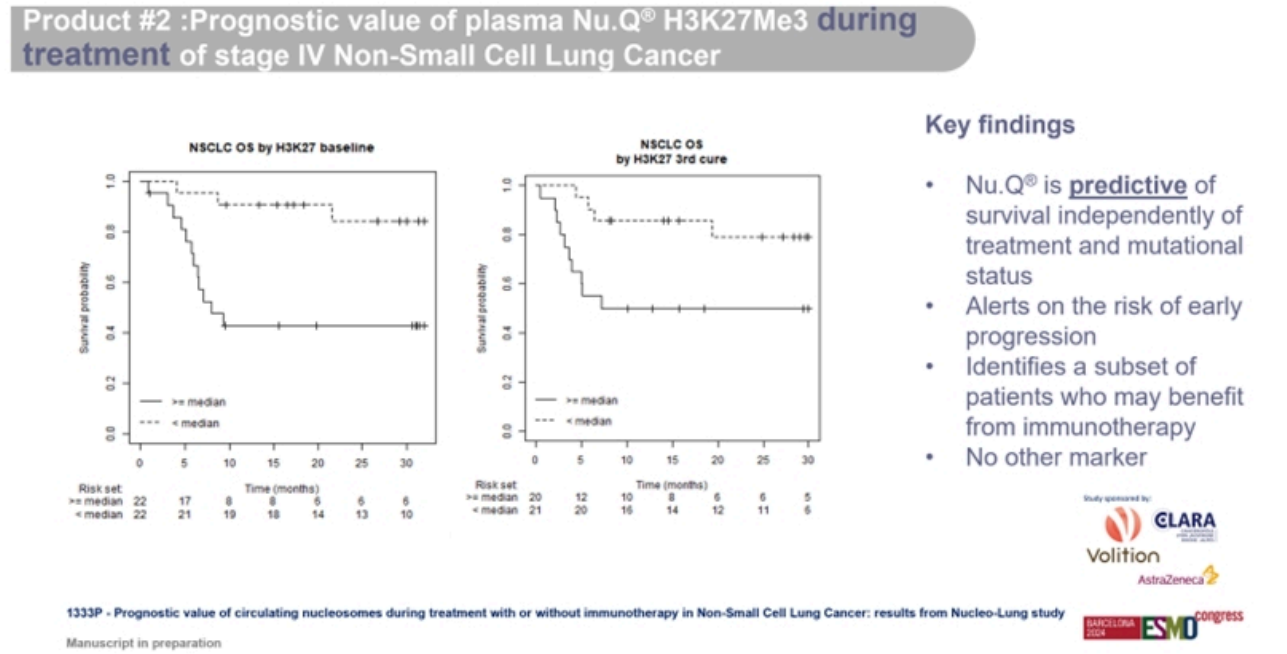


Source: VolitionRx presentation, April 2025

Exhibit 9 above shows data from the NUCLEO-LUNG study presented at the European Lung Cancer Congress 2024.

In this study, nucleosome levels of patients with Stage IV NSCLC were measured. Study data revealed that patients with low H3K27Me3 at baseline in a palliative cohort (n=19) had longer survival times based on the Kaplan-Meier curve compared to those with higher values (n=30) in the same palliative cohort, suggesting this arm (low H3K27Me3) would derive more benefit from additional curative therapy (eg immunotherapy) attempts.

Exhibit 10: NUCLEO-LUNG shows prognostic value of H32K27Me3 levels during treatment

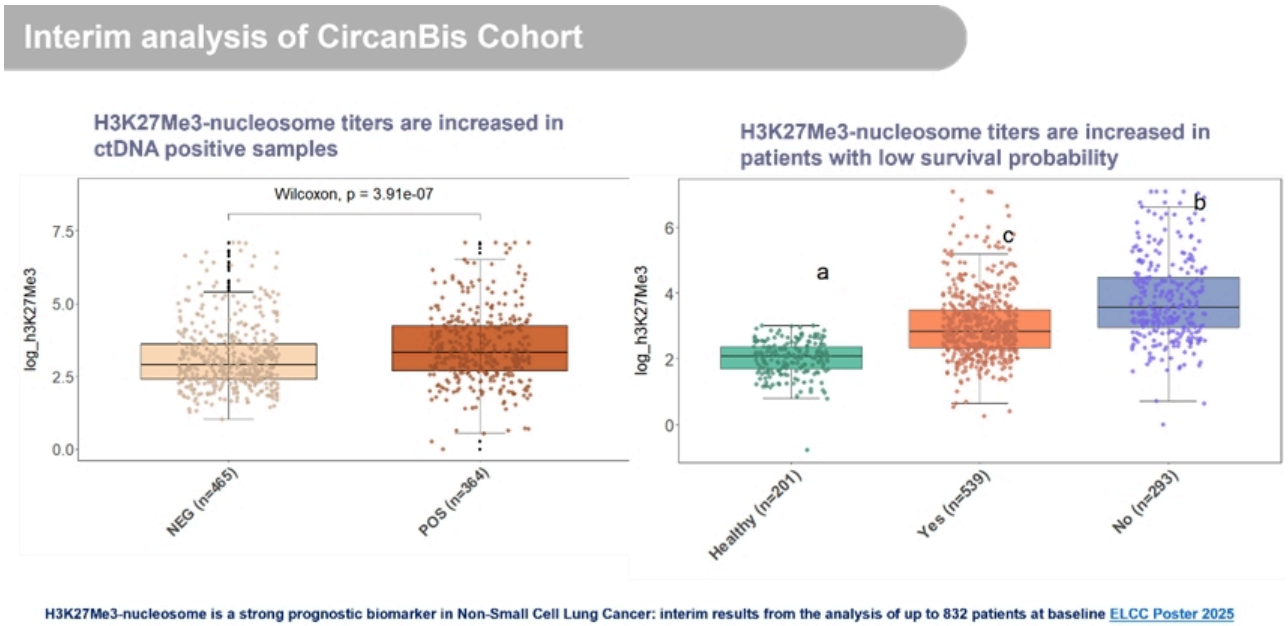


Source: VolitionRx presentation, April 2025

Further information from the NUCLEO-LUNG study (Exhibit 10) shows that H3K27Me3 scores taken from Stage IV NSCLC patients undergoing ongoing cancer treatment were predictive of overall survival. The chart on the left shows that patients with lower H3K27Me3 scores (below the median value among the cohort) at baseline had a significantly higher survival probability than those with higher H3K27Me3 scores at baseline. The chart on the right shows a similar separation (between high and low H3K27Me3 scores) with the sample measures taken later during treatment. The conclusion is that H3K27Me3 is inversely correlated with survival, and for patients undergoing treatment, elevated levels can provide an indication that a change of treatment (or additional therapy) may be warranted (supporting the basis for Product 3). Nu.Q H3K27Me3 level is shown to be predictive of survival independently of treatment and mutational status.

Relating to the above findings, the larger-scale CircanBis study was conducted in Lyon, France, and assessed and monitored 1,050 patients with NSCLC, where blood samples were taken at baseline. Molecular profiling of ctDNA was performed using NGS, and H3K27Me3-nucleosome titers were assessed using Volition's Nu.Q immunoassay. A retrospective analysis on interim data (n=832) was reported in March 2025, and was performed to evaluate the predictive capabilities of these biomarkers in anticipating outcomes when used alongside the current gold standard of measuring and profiling ctDNA at baseline or at diagnosis. In particular, the analysis found that when combined with ctDNA, H3K27Me3 levels improve the prognostic value for overall survival and could help inform treatment decisions. H3K27Me3-nucleosome titers are found to be increased in ctDNA positive samples, as shown in Exhibit 11, but more importantly, and similar to the NUCLEO-LUNG study data above, the H3K27Me3 titers are higher in patients with lower survival rates and probabilities, independent of the molecular profiling results shown on ctDNA analysis.

Exhibit 11: Interim CircanBis data showing H3K27Me3 correlations



Source: Volition, April 2025 Presentation and ELCC Congress Poster

Exhibit 12 provides more granularity on the H3K27Me3 data correlations. Effectively, the mean survival of the low H3K27Me3 group (Chart B) was 24.7 months versus 11.2 months in those with the high H3K27Me3 group. Among patients with ctDNA+ readings (Chart C), the mean survival was 22.3 months in those with low H3K27Me3 versus 12.8 months in the high nucleosome group. Among patients with ctDNA- findings (Chart D), the low H3K27Me3 cohort had a mean survival of 27.4 months versus 13.4 months for the high H3K27Me3 cohort.

Exhibit 12: Interim CircanBiS survival rates by ctDNA status and H3K27Me3 titers

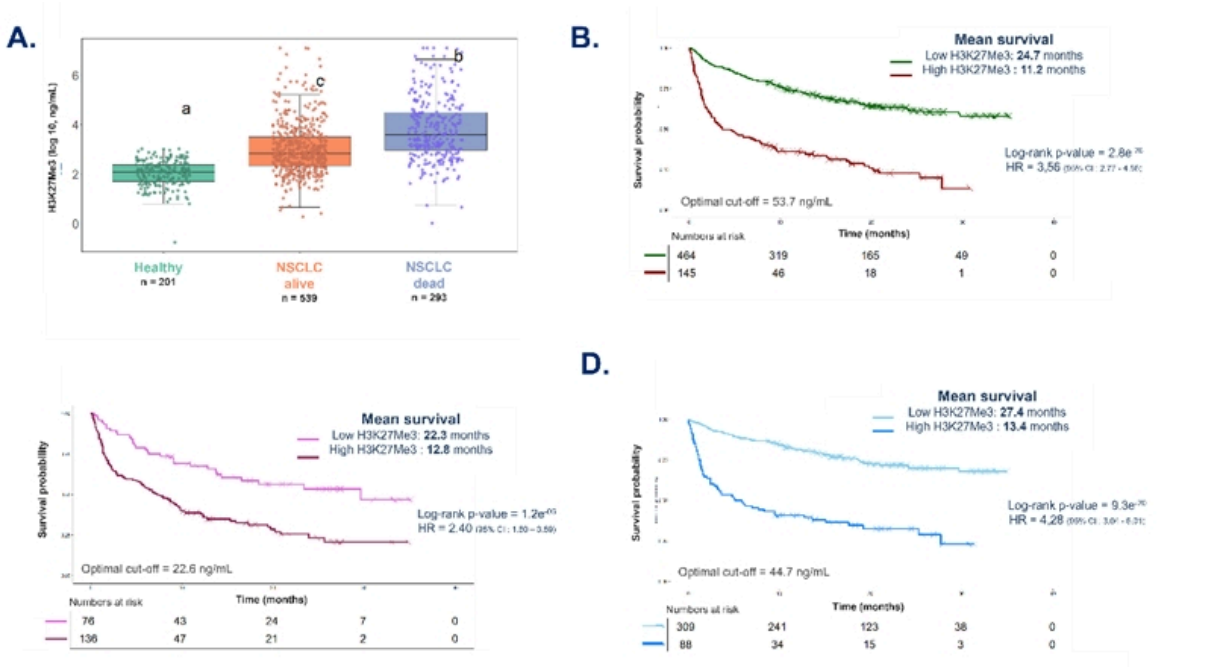


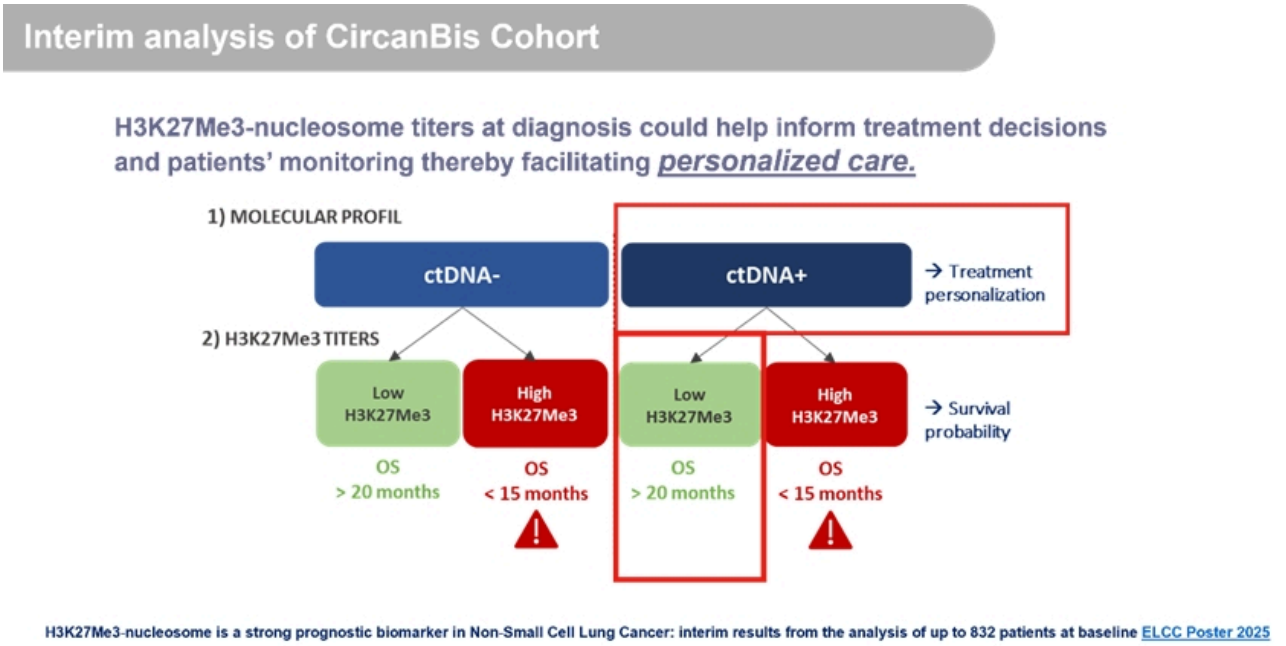
Figure 2
(A) H3K27Me3-nucleosome blood titers in cancer patients at diagnosis according to survival status (orange = alive, median 17.03 ng/mL vs blue = dead, median 35.49 ng/mL) compared to a healthy cohort (green, median 8.0 ng/mL). (B) Survival analysis according H3K27Me3-nucleosomes titers at diagnosis (optimal cut-off 53.7 ng/mL). (C) Overall survival according to H3K27Me3-nucleosomes titers in patients with at least one somatic mutation detected on ctDNA (ctDNA+, optimal cut-off = 22.6 ng/mL). (D) Overall survival of patients with negative molecular profiling (ctDNA-) according to H3K27Me3-nucleosomes titers (optimal cut-off = 44.7 ng/mL).

Source: ELCC Congress Poster, March 2025. VolitionRx

Overall, the CircanBis interim data confirm that nucleosome variant H3K27me3 is a non-invasive biomarker in NSCLC

patients that predicts survival regardless of ctDNA mutation status. This assay data can be obtained through Nu.Q. Product 2 and then be used in a treatment decision paradigm, as demonstrated in Exhibit 13.

Exhibit 13: Treatment decision tree (for Nu.Q Product 2)



Source: Volition, April 2025 presentation and ELCC congress poster

The decision tree shows how Product 2 can be used to determine H3K27Me3 status in patients with late-stage NSCLC where the disease has advanced despite prior therapies. Regardless of ctDNA mutational status, patients with low H3K27Me3 levels may benefit from additional and personalized therapy (given the higher expected survival rate), whereas patients with higher levels may be better suited for palliative care (given the lower expected survival). Full CircanBis data are expected in mid-2025, but we anticipate the data are likely to confirm the trends shown above, given that the majority of recruited patients (832 of 1,050) have been analyzed in the interim data.

VolitionRx and its collaborators are currently undertaking the ULYSEE Map study (Lyon, France) on 100 patients; it is a prospective study to assess H3K27Me3 for prognostics (survival prediction) and also assess patients for MRD. Results are expected in Q425.

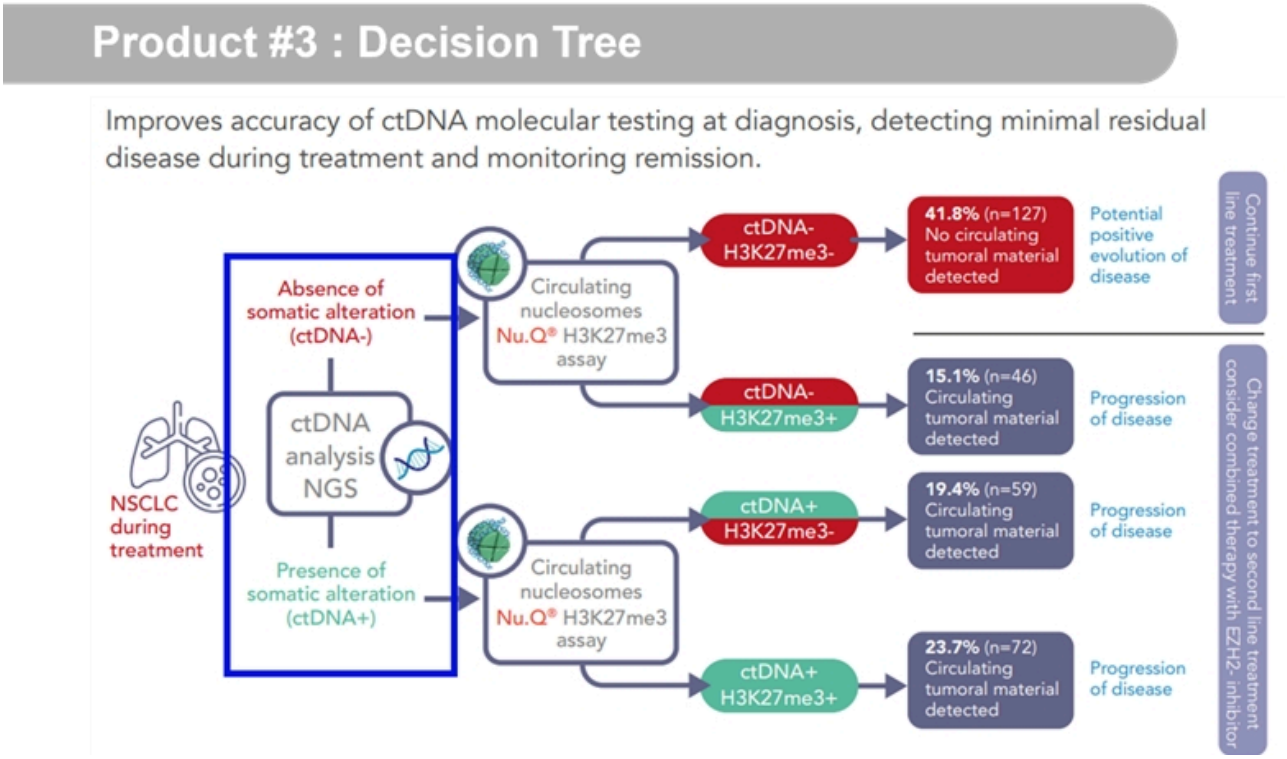
Product 3 uses nucleosome data to assess therapy effectiveness

Product 3, which is also based on Nu.Q H3K27Me3 assay, aims to use a drawn blood sample to improve the accuracy of detecting MRD during treatment and for monitoring remission in lung cancer patients. The intent is to provide better accuracy in assessing MRD than using ctDNA alone.

During cancer treatment, if a patient is tested for ctDNA using NGS and the result is negative (ctDNA-) and H3K27me3 levels are low, the interpretation is that no circulating tumoral material is being detected. This suggests favorable management of the disease (ie either the current treatment is effective, or the patient remains in remission).

However, if ctDNA is positive or H3K27me3 is elevated, this suggests that circulating tumoral material is detected in the bloodstream, and that there may be progression of disease that warrants a change in the treatment plan.

Exhibit 14: Product 3 decision tree



Source: VolitionRx presentation, April 2025

The Nu.Q product assays for lung cancer all measure H3K27Me3 levels in the bloodstream, and aim to cover the full range of the lung cancer management pathway as described in Exhibit 3. Product 1 measures baseline H3.1 and H3K27Me3 to improve diagnostics and reduce the reliance on invasive biopsies. Product 2 aims to identify which late-stage lung cancer patients may benefit from additional therapy versus those better suited to palliative care. As stated above, Product 3 is designed to be used in lung cancer patients undergoing treatment, and aims to provide clinicians with key information on whether the chosen treatment plan is working as planned, and to provide stronger differentiation than relying on ctDNA status findings alone.

Summary

As the health burden of cancer continues to grow, the need for effective diagnosis and monitoring is gaining prominence. While certain cancer indications, such as breast and colorectal cancer, have seen widespread adoption of early screening tests (which have also demonstrated a positive impact on reducing mortality), lung cancer screening with LDCT, despite showing promise, has continued to face challenges in terms of awareness, eligibility criteria and adherence rates. LDCT alone, while highly sensitive in detecting potential cancers, lacks optimal specificity when used on its own, and which is why positive findings have often resulted in unnecessary tissue biopsies. The need for more cost-effective, non-invasive diagnostics approaches that reduces the need for biopsies continues to be felt more acutely in this space, in particular given the high mortality rates (1.8 million deaths globally per year). We believe that a simple, non-invasive blood test, such as Nu.Q Cancer, offers an attractive alternative to the more complex NGS-based molecular testing tools currently in development for lung cancer.

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