

Exemplary Embodying Product Claim Chart for U.S. Patent No. 11,299,783 (the “783 Patent”)

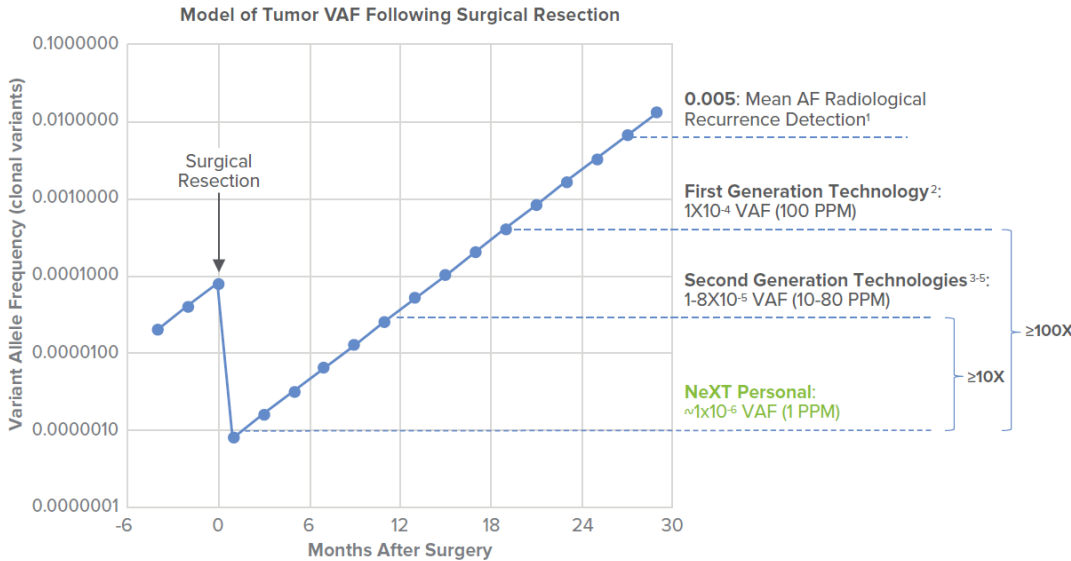
Personalis reserves the right to rely upon expert testimony and/or analysis and to amend this chart as necessary

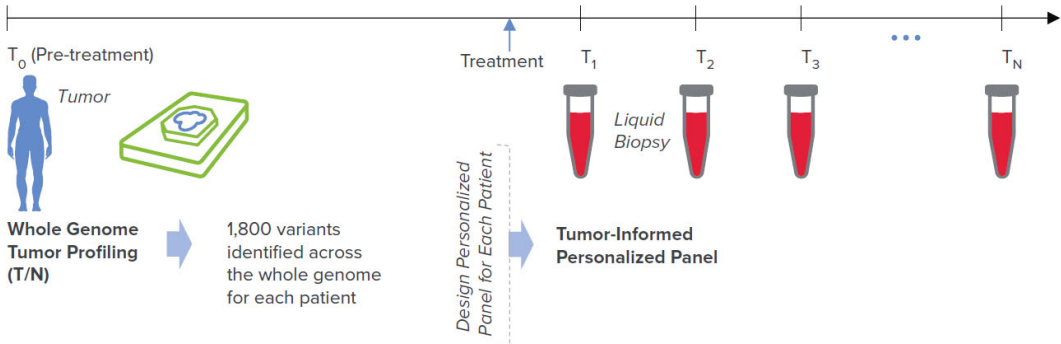
'783 Patent Claim Language	NeXT Personal™ Test
1. A method for personalized genetic testing, comprising:	The Next Personal Test performs a method for personalized genetic testing. Delivering Industry-Leading Sensitivity to Detect Residual Disease at the Earliest Timepoints NeXT Personal, an advanced, personalized, and tumor-informed liquid biopsy assay, is designed to detect molecular residual disease (MRD) and cancer recurrence at the earliest timepoints — prior to, during or after treatment — in patients previously diagnosed with cancer. While circulating tumor-derived DNA (ctDNA) is an emerging biomarker for many cancers, the limited sensitivity of current detection methods reduces its utility for diagnosing MRD across a variety of clinical applications. Standard-of-care (SOC) radiological-based technologies, including CT, PET and MRI scans, also remain limited in their ability to detect residual disease during or after surgical or systemic therapy due to the minimum tumor volume required.¹ Therefore reliable, sensitive detection and quantification of MRD remains a key challenge, particularly in early-stage cancers, where timely detection of small micrometastatic lesions may enable treatment that prevents progression to advanced metastatic, incurable disease. To address these challenges, NeXT Personal was developed to deliver industry-leading MRD sensitivity in the range of 1-3 parts per million (PPM) representing a 10-100X increase over other available methods (Figure 1), while requiring only a single tube of blood (4mL plasma/15ng cfDNA), and 1mm³ of FFPE tumor tissue. Source: Exh. 1 - Personalis NeXT Personal Brochure, p.1
(a) obtaining a personalized probe set for a subject, which personalized probe set comprises a plurality of nucleic acid probe molecules having a plurality of nucleic acid sequences or complements thereof, wherein said plurality of nucleic acid probe molecules are configured to selectively enrich or amplify sequences	The method of conducting the NeXT Personal test involves contacting nucleic acid samples with capture probes, which are configured to selectively amplify sequences with particular genetic variants in a biological sample.

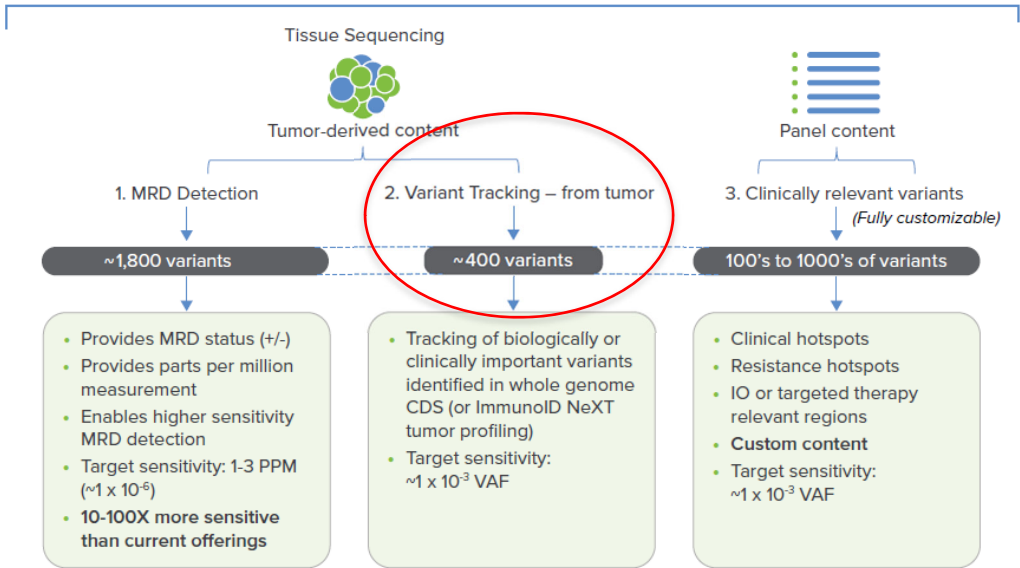
'783 Patent Claim Language	NeXT Personal™ Test
comprising a set of one or more genetic variants over other sequences in at least one biological sample of said subject, wherein said set of genetic variants are identified in sequence data for said at least one biological sample, further wherein said personalized probe set comprises nucleic acid probe molecules having oligonucleotide-directed genomic content comprising: (i) at least one variable portion from a result of said sequence data and (ii) at least one fixed portion independent of said result of said sequencing data	6. As background, both Foresight and Personalis offer testing products that can be used to monitor for cancer recurrence by detecting and analyzing tiny amounts of tumor DNA that are present in the bloodstream of a cancer patient. It is important to understand that both Foresight and Personalis offer testing products that operate according to the same basic principles, specifically, by using whole genome sequencing of a tumor sample to identify mutations that can subsequently be detected in circulating tumor DNA by capturing the mutation carrying DNA with capture probes and then sequencing the captured DNA. This unique approach distinguishes the Foresight and Personalis tests from other testing products, and allows the products from Foresight and Personalis to achieve greater sensitivity relative to other testing products currently on the market. Source: Exh. 2 - Case No. 1:22-cv-01913, Dkt. 42, Ex. B (Mouradian Decl.) at ¶¶6 The NeXT Personal Test involves using personalized probes as well as known cancer-related clinical variants.

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	Here we report a performance update of the NeXT Personal® platform. NeXT Personal utilizes hybridization-capture-based technology to quantify ctDNA in liquid biopsy samples. Its unified probe panel design and workflow simultaneously detects and monitors MRD, surveys known cancer-related clinical variants, and quantifies and tracks investigational variants of interest, by leveraging both tumor-informed and tumor-agnostic genomic information (Fig. 1). The tumor-informed MRD content is dedicated to personalized MRD detection and longitudinal monitoring, which utilizes cumulative tumor-derived signals to achieve ultra-high sensitivity down to 1 ~ 3 parts per million (PPM) limit of detection (LOD). The tumor-agnostic clinically relevant content surveys known and validated actionable genomic variants in 90 clinically relevant genes, and serves to inform therapy selection and detect existing or potentially emerging events such as new subclones or metastases. The investigational content provides capacity to track important cancer-related variants for research or investigational purposes. Source: Exh. 3 – Analytical performance of an ultra-sensitive, tumor-informed liquid biopsy platform for molecular residual disease detection and clinical guidance. The NeXT Personal test also detects SNVs at >30x WGS coverage of a patient's tumor. This translates into sequencing over 90 gigabases. Leveraging Tissue-Based Whole Genome Sequencing (WGS) Yields Best-In-Class MRD Performance in Plasma: 1-3 PPM Sensitivity Central to the MRD performance of NeXT Personal is the number of tumor-derived mutations interrogated in patient plasma samples. Analytical and clinical MRD sensitivity can be increased by expanding coverage of loci containing tumor-specific mutations.⁷ To this end, NeXT Personal leverages the broad array of SNVs detected with >30x WGS coverage of a patient's tumor (and accompanying normal) to inform the selection of 1,800 SNVs for inclusion in a personalized MRD panel (Figure 3). The majority of these patient-specific SNVs are located in non-coding regions of the genome. Finally, Personalis' extensive investment into the Illumina® NovaSeq® series enables ultra-deep sequencing (~100,000 raw depth), while keeping costs in line with other MRD tests that interrogate many fewer loci. Source: Exh. 1 - Personalis NeXT Personal Brochure, p. 6.
(b) using said personalized probe set to	The capture probes selectively amplify sequences comprising the set of genetic

'783 Patent Claim Language	NeXT Personal™ Test
selectively enrich or amplify sequences comprising said set of genetic variants over other sequences in at least an additional biological sample from said subject, to generate a sequencing library;	variants over other sequences in additional biological samples taken from the subject, perhaps post-surgery, to generate a sequencing library 6. As background, both Foresight and Personalis offer testing products that can be used to monitor for cancer recurrence by detecting and analyzing tiny amounts of tumor DNA that are present in the bloodstream of a cancer patient. It is important to understand that both Foresight and Personalis offer testing products that operate according to the same basic principles, specifically, by using whole genome sequencing of a tumor sample to identify mutations that can subsequently be detected in circulating tumor DNA by capturing the mutation carrying DNA with capture probes and then sequencing the captured DNA. This unique approach distinguishes the Foresight and Personalis tests from other testing products, and allows the products from Foresight and Personalis to achieve greater sensitivity relative to other testing products currently on the market. Source: Exh. 2 - Case No. 1:22-cv-01913, Dkt. 42, Ex. B (Mouradian Decl.) at ¶¶6 Fig. 1 shows the tracking of tumor variant allele frequencies in the subsequently analyzed samples from additional time points.

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	Figure 1: MRD Sensitivity: Targeting Detection at Earliest Timepoints  Model Assumptions: Median breast tumor size detected by mammography: 1.3cm, Median shedding per NSCLC TRACERx study⁶; Residual tumor from surgery: 1%; Volume doubling time (actual VAF time): 2 months Source: Personalis NeXT Personal Brochure, Figure 1
(c) subjecting said sequencing library to sequencing to identify a presence or absence of at least a subset of said set of genetic variants in at least said additional biological sample from said subject, wherein a sequencing footprint of said sequencing of (c) is less than a sequencing footprint of said sequence	The NeXT Personal test involves sequencing the sequencing library to identify a subset of genetic variants in the additional biological sample.

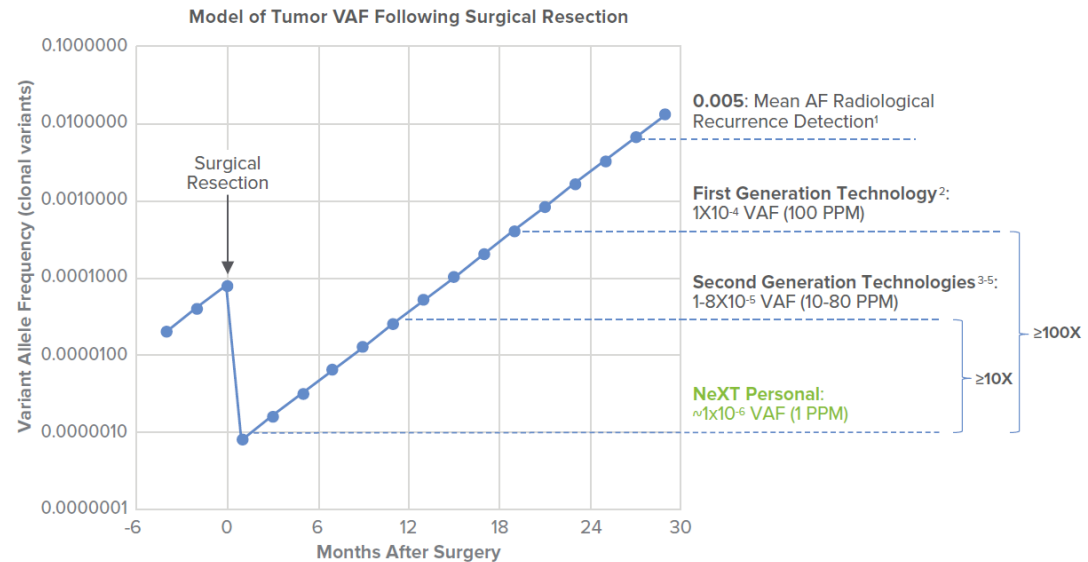
'783 Patent Claim Language	NeXT Personal™ Test
data of (a); and	Figure 3: NeXT Personal: Advanced, Higher Sensitivity, Personalized, Tumor-Informed Liquid Biopsy for MRD & Variant Tracking  Source: Personalis NeXT Personal Brochure, Figure 3. Leveraging Tissue-Based Whole Genome Sequencing (WGS) Yields Best-In-Class MRD Performance in Plasma: 1-3 PPM Sensitivity Central to the MRD performance of NeXT Personal is the number of tumor-derived mutations interrogated in patient plasma samples. Analytical and clinical MRD sensitivity can be increased by expanding coverage of loci containing tumor-specific mutations.⁷ To this end, NeXT Personal leverages the broad array of SNVs detected with >30x WGS coverage of a patient's tumor (and accompanying normal) to inform the selection of 1,800 SNVs for inclusion in a personalized MRD panel (Figure 3). The majority of these patient-specific SNVs are located in non-coding regions of the genome. Finally, Personalis' extensive investment into the Illumina® NovaSeq® series enables ultra-deep sequencing (~100,000 raw depth), while keeping costs in line with other MRD tests that interrogate many fewer loci. Source: Personalis NeXT Personal Brochure, p. 6. The NeXT Personal test also involves a variant tracking panel that identifies a subset of ~400 sequences, with a sequencing coverage footprint that is less than the sequencing footprint of the sequence data in step (a)

'783 Patent Claim Language	NeXT Personal™ Test
	Figure 2: NeXT Personal Assay Features: Advanced, higher sensitivity, personalized, tumor-informed liquid biopsy for MRD & Variant Tracking One Assay. Multiple Functions.  <pre> graph TD TS[Tissue Sequencing] --> TDC[Tumor-derived content] TS --> PC[Panel content] TDC --> MRD[1. MRD Detection] TDC --> VT[2. Variant Tracking – from tumor] PC --> CRV[3. Clinically relevant variants (Fully customizable)] MRD --> V1[~1,800 variants] VT --> V2[~400 variants] CRV --> V3[100's to 1000's of variants] V1 --> F1[Provides MRD status +/- Provides parts per million measurement Enables higher sensitivity MRD detection Target sensitivity: 1-3 PPM (~1 x 10^-6) 10-100X more sensitive than current offerings] V2 --> F2[Tracking of biologically or clinically important variants identified in whole genome CDS (or Immunoid NeXT tumor profiling) Target sensitivity: ~1 x 10^-3 VAF] V3 --> F3[Clinical hotspots Resistance hotspots IO or targeted therapy relevant regions Custom content Target sensitivity: ~1 x 10^-3 VAF] </pre> Source: Exh. 1 - Personalis NeXT Personal Brochure, Fig. 2.
(d) generating a report identifying (i) a presence or absence of a health condition or disease of the subject in said additional biological sample based on said identified at least a subset of (c) and (ii) genetic variants which inform a therapy choice or a change in therapy for the subject.	The NeXT Personal test generates a biomedical report that includes biomedical information, including the presence or absence of polymorphisms identified in the prior sequencing of the plasma samples. For example, NeXT Personal test shows in Fig. 1 shows the tracking of tumor variant allele frequencies in the subsequently analyzed samples from additional time points.

'783 Patent Claim Language

NeXT Personal™ Test

Figure 1: MRD Sensitivity: Targeting Detection at Earliest Timepoints



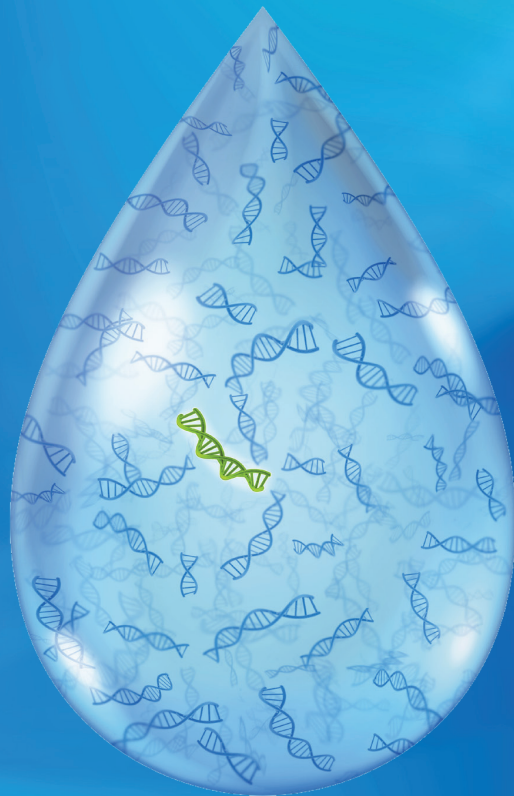
Model Assumptions: Median breast tumor size detected by mammography: 1.3cm, Median shedding per NSCLC TRACERx study⁶; Residual tumor from surgery: 1%; Volume doubling time (actual VAF time): 2 months

Source: Personalis NeXT Personal Brochure, Figure 1

The identified genetic variants are used to inform the understanding of the tumor biology and its dynamic response to therapy

'783 Patent Claim Language	NeXT Personal™ Test
	Unique Assay Design Provides Unprecedented Insights Into Longitudinal Disease Monitoring While the MRD component of NeXT Personal provides a highly sensitive and aggregated measurement of tumor burden in plasma, the ability to simultaneously track individual variants longitudinally can also be utilized to further our understanding of tumor biology and its dynamic response to therapy. Therefore, in addition to MRD, NeXT Personal provides the ability to track and annotate individual variants over the whole evolution of a cancer patient's trajectory in a single panel design. Variants tracked by NeXT Personal in the blood are derived from those detected in the tissue, as well as those specified for panel inclusion by the user (Figure 2). Figure 2: NeXT Personal Assay Features: Advanced, higher sensitivity, personalized, tumor-informed liquid biopsy for MRD & Variant Tracking One Assay. Multiple Functions. <pre> graph TD TS[Tissue Sequencing] --> TDC[Tumor-derived content] TS --> PC[Panel content] TDC --> MRD[1. MRD Detection] TDC --> VT[2. Variant Tracking – from tumor] PC --> CRV[3. Clinically relevant variants (Fully customizable)] MRD --> V1[~1,800 variants] VT --> V2[~400 variants] CRV --> V3[100's to 1000's of variants] V1 --> B1[Provides MRD status +/- Provides parts per million measurement Enables higher sensitivity MRD detection Target sensitivity: 1-3 PPM (~1 x 10⁻⁶) 10-100X more sensitive than current offerings] V2 --> B2[Tracking of biologically or clinically important variants identified in whole genome CDS (or Immunoid NeXT tumor profiling) Target sensitivity: ~1 x 10⁻³ VAF] V3 --> B3[Clinical hotspots Resistance hotspots IO or targeted therapy relevant regions Custom content Target sensitivity: ~1 x 10⁻³ VAF] </pre> Source: Personalis NeXT Personal Brochure, Figure 2

EXHIBIT 1



NeXT Personal™

The Next Generation in Molecular Residual Disease
Testing and Variant Monitoring for Solid Tumors



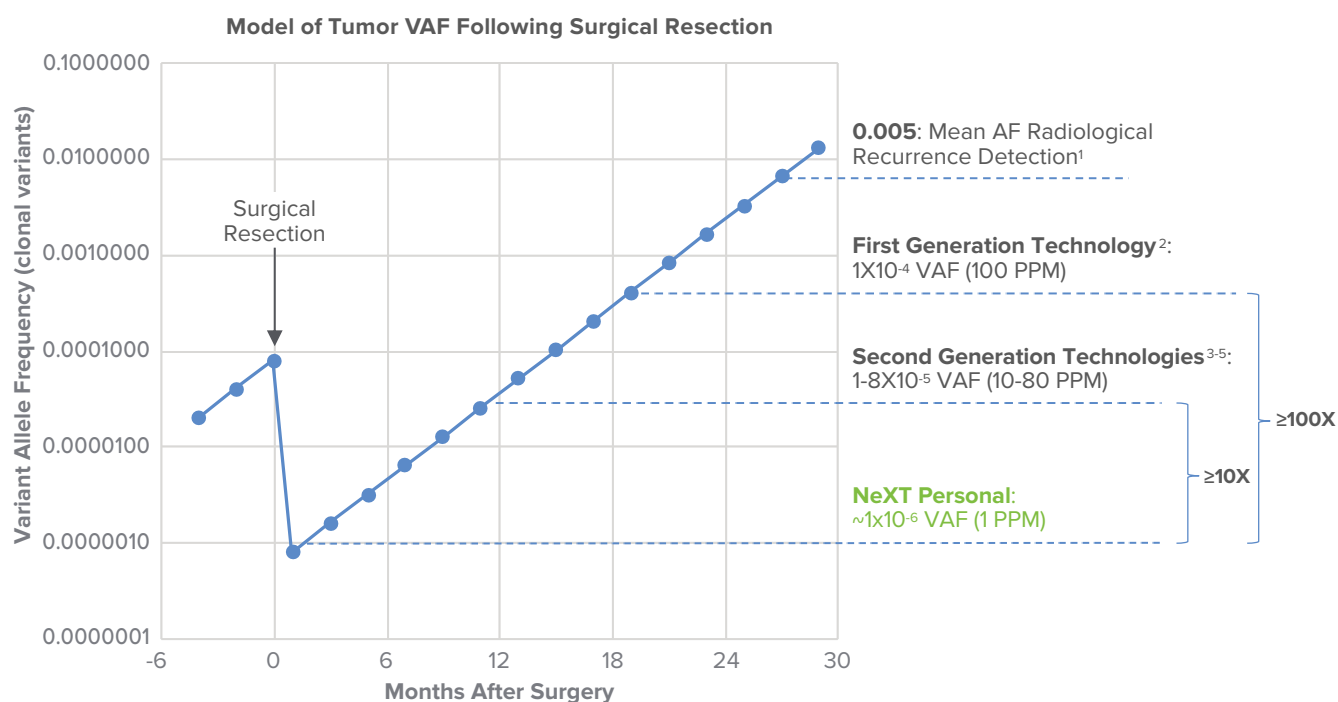
**Personalis Ex. 2003.011
Foresight v. Personalis
IPR2023-00545**



Delivering Industry-Leading Sensitivity to Detect Residual Disease at the Earliest Timepoints

NeXT Personal, an advanced, personalized, and tumor-informed liquid biopsy assay, is designed to detect molecular residual disease (MRD) and cancer recurrence at the earliest timepoints — prior to, during or after treatment — in patients previously diagnosed with cancer. While circulating tumor-derived DNA (ctDNA) is an emerging biomarker for many cancers, the limited sensitivity of current detection methods reduces its utility for diagnosing MRD across a variety of clinical applications. Standard-of-care (SOC) radiological-based technologies, including CT, PET and MRI scans, also remain limited in their ability to detect residual disease during or after surgical or systemic therapy due to the minimum tumor volume required.¹ Therefore reliable, sensitive detection and quantification of MRD remains a key challenge, particularly in early-stage cancers, where timely detection of small micrometastatic lesions may enable treatment that prevents progression to advanced metastatic, incurable disease. To address these challenges, NeXT Personal was developed to deliver industry-leading MRD sensitivity in the range of 1-3 parts per million (PPM) representing a 10-100X increase over other available methods (Figure 1), while requiring only a single tube of blood (4mL plasma/15ng cfDNA), and 1mm³ of FFPE tumor tissue.

Figure 1: MRD Sensitivity: Targeting Detection at Earliest Timepoints



Model Assumptions: Median breast tumor size detected by mammography: 1.3cm, Median shedding per NSCLC TRACERx study⁶; Residual tumor from surgery: 1%; Volume doubling time (actual VAF time): 2 months

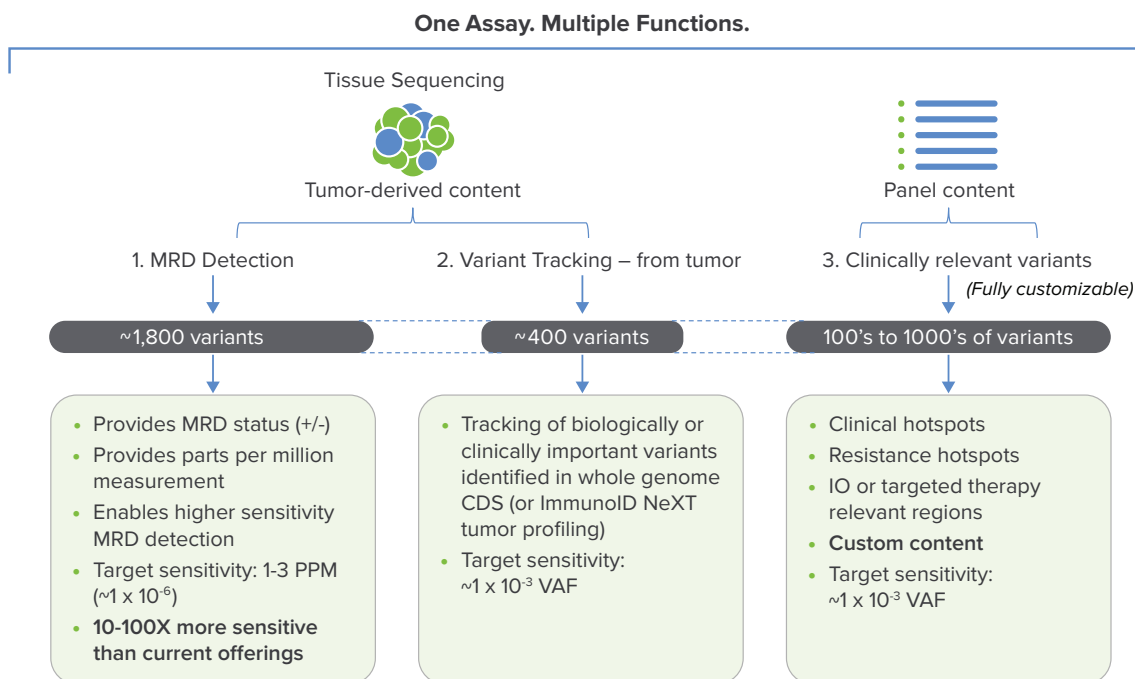
In the biopharma setting, MRD is rapidly emerging as a key biomarker in therapy development, whereby more sensitive detection and quantification of MRD may provide substantial benefits versus less sensitive methods through the reduction of false negative detection of cancer. These benefits include:

- More efficient cohort enrichment of study participants that are MRD positive.
- Faster time to surrogate endpoint analysis through earlier detection of MRD.
- Enhanced accuracy of recurrence and survival risk.
- Greater resolution of therapy response.

Unique Assay Design Provides Unprecedented Insights Into Longitudinal Disease Monitoring

While the MRD component of NeXT Personal provides a highly sensitive and aggregated measurement of tumor burden in plasma, the ability to simultaneously track individual variants longitudinally can also be utilized to further our understanding of tumor biology and its dynamic response to therapy. Therefore, in addition to MRD, NeXT Personal provides the ability to track and annotate individual variants over the whole evolution of a cancer patient's trajectory in a single panel design. Variants tracked by NeXT Personal in the blood are derived from those detected in the tissue, as well as those specified for panel inclusion by the user (Figure 2).

Figure 2: NeXT Personal Assay Features: Advanced, higher sensitivity, personalized, tumor-informed liquid biopsy for MRD & Variant Tracking



For every panel, NeXT Personal boasts the capacity to include up to 400 single nucleotide variants (SNVs) detected in the tumor to track in plasma. NeXT Personal automatically filters for variants that lie in coding regions of clinically relevant genes, prioritizing those in genes with known relevance to cancer. This ensures that the most biologically and clinically important variants are tracked longitudinally to deliver insights on evolving tumor biology (Figure 2.2).

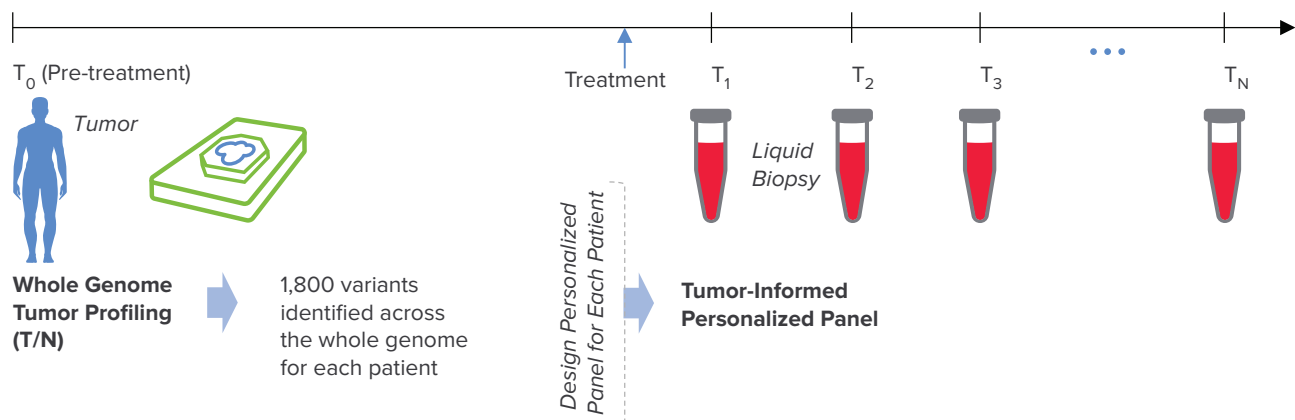
Similarly, variants not detected in the tumor may also be added during the panel design process. As custom content, users may define their own set of variants that may be representative of known clinical hotspots (ex. EGFR T790M), resistance hotspots, driver mutations (which may allow detection of a second primary tumor), or other therapy-specific and biologically important variants studied or monitored in clinical research. Capacity for user-supplied content can include up to thousands of variants. Alternatively, users may also leverage clinically relevant content developed and curated by Personalis in addition to, or instead of, user-supplied content (Figure 2.3).

Target sensitivity for individual variant detection is 0.1% VAF.

Leveraging Tissue-Based Whole Genome Sequencing (WGS) Yields Best-In-Class MRD Performance in Plasma: 1-3 PPM Sensitivity

Central to the MRD performance of NeXT Personal is the number of tumor-derived mutations interrogated in patient plasma samples. Analytical and clinical MRD sensitivity can be increased by expanding coverage of loci containing tumor-specific mutations.⁷ To this end, NeXT Personal leverages the broad array of SNVs detected with >30x WGS coverage of a patient's tumor (and accompanying normal) to inform the selection of 1,800 SNVs for inclusion in a personalized MRD panel (Figure 3). The majority of these patient-specific SNVs are located in non-coding regions of the genome. Finally, Personalis' extensive investment into the Illumina® NovaSeq® series enables ultra-deep sequencing (~100,000 raw depth), while keeping costs in line with other MRD tests that interrogate many fewer loci.

Figure 3: NeXT Personal: Advanced, Higher Sensitivity, Personalized, Tumor-Informed Liquid Biopsy for MRD & Variant Tracking



Upon completion of sequencing with the tumor-informed personalized panel, data generated across these 1,800 targeted loci are analyzed and an aggregated measurement of tumor burden is reported in a PPM readout with accompanying MRD status (MRD+/-). Rather than using a predetermined minimum number of mutations to define MRD status, NeXT Personal uses advanced, proprietary statistical analyses to distinguish signal from noise for each individual patient panel and sample. Guided by a P-value threshold of <0.001 (derived from a specificity target of $>99.9\%$), NeXT Personal is optimized for both sensitivity and specificity.

Assessing the prospective utility of individual MRD targets is an important aspect of tumor-informed panel design. Tissue WGS often yields tens of thousands of mutations, but selecting those that are most likely to be (1) shed into the blood and (2) have high signal-to-noise profiles is of critical importance. While the human genome harbors a plethora of inherently noisy regions, Personalis, leveraging its extensive experience with WGS, is the first company to develop methods to filter for targets that may be difficult to resolve if detected in plasma. Further, the abundance of variants identified via WGS allows the selection of predominately truncal mutations with high allele frequencies; those that are more likely to be shed into the blood.

The powerful combination of WGS to enable target breadth, coupled with robust error and noise reduction methods, results in MRD sensitivity in the 1-3 PPM range with $\geq 99.9\%$ specificity (Figures 4 and 5).

Figure 4: Cell line dilution series, HCC38, demonstrates the linearity of tumor signal across the dilution series down to the 1-3PPM range (C50 and C95, respectively). Orthogonal confirmation using droplet digital PCR (ddPCR) demonstrates near-perfect concordance down to ddPCR LOD (750 PPM).

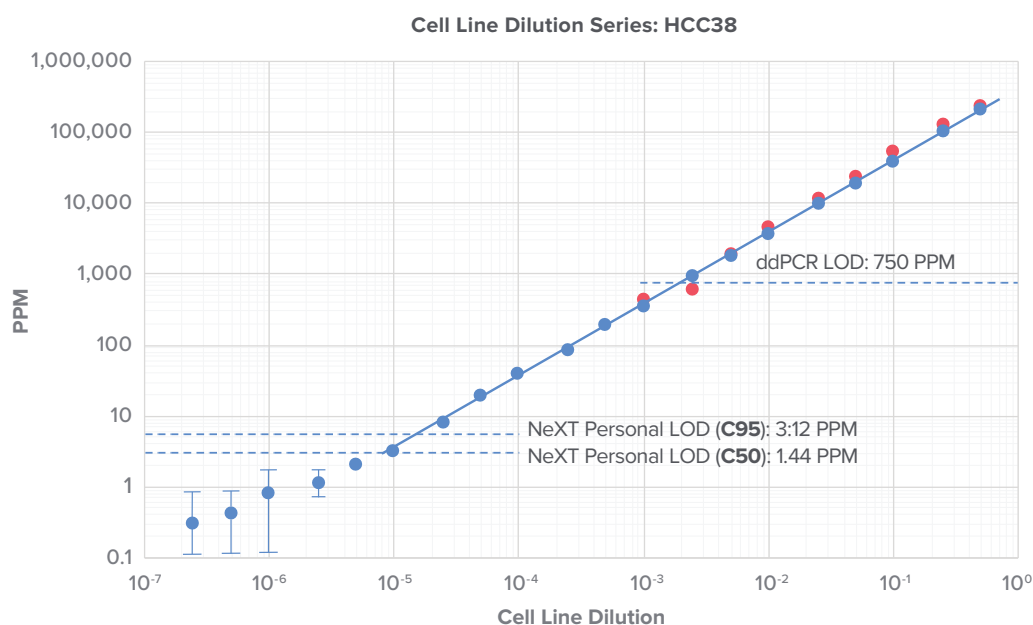
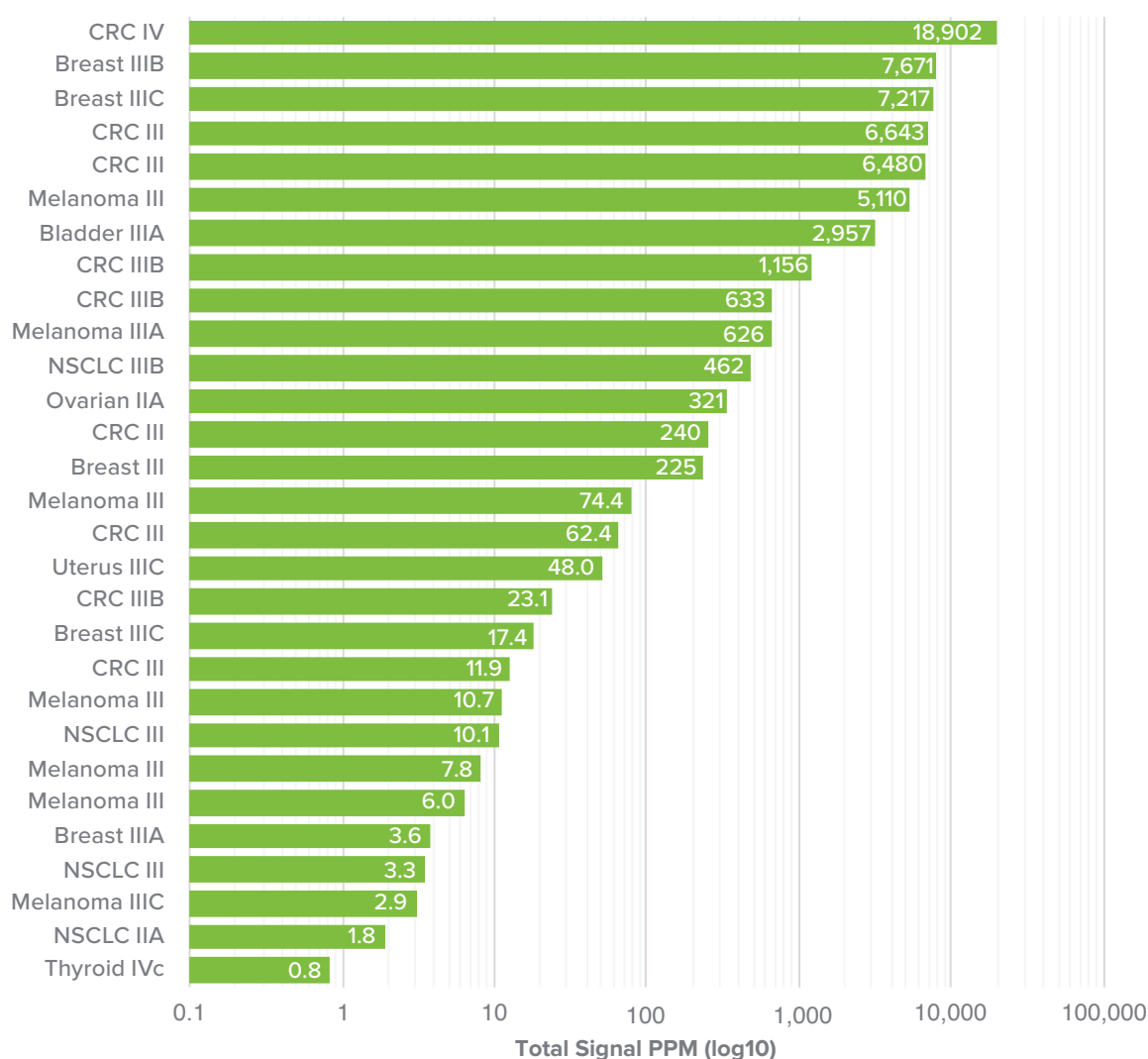


Figure 5: Patient T/N/P trios across 8 tumor types and 3 stages were sequenced demonstrating range of detection; 0.8 – ~19,000 PPM



Target Breadth Mitigates Challenging Sample Conditions

Target breadth is important to achieve higher sensitivity, but it is also important to overcome challenging sample conditions. The success of tumor-informed liquid biopsy approaches is dependent on the number of targeted mutant fragments present in the sample. Key variables that determine successful MRD detection are: (1) number of genomic equivalents (GEs) in the plasma sample, (2) tumor fraction in the plasma sample, and (3) tumor mutational burden (TMB) in the tissue sample. Under ideal sample conditions — characterized by a high number of GEs in plasma, a high tumor fraction in plasma, and a high TMB in tissue — narrower tumor-informed panel footprints (ex. those constrained by the tissue exome-seq) and fixed content panels may be sufficient to detect MRD.

However, ideal sample conditions are often not attainable:

- Tumor fraction in plasma in early-stage cancers is often low due to limited shedding of DNA molecules from small, localized lesions.⁸
- Plasma volume can be difficult to obtain due to patient variability, study design, and other blood analyte testing requirements.
- Finally, tissue TMB is highly variable and less dependent on tumor type and tumor stage⁹, with low TMB tumors reducing the number of high-quality variant candidates for MRD panel inclusion, materially impacting assay performance.

NeXT Personal mitigates these challenges by ensuring high coverage (1,800 loci) of the tumor-derived DNA molecules, increasing the detection probability of mutant fragments even when there are few. Therefore, even in challenging sample conditions, NeXT Personal is able to deliver superior assay performance.

Combining ImmunID NeXT™ and NeXT Personal Yields Multidimensional View Into Tumor Biology

In addition to NeXT Personal, Personalis' flagship tissue-based immunogenomics platform, ImmunID NeXT, may also be run from the same tissue sample with no additional tumor material required. For the first time, investigators can comprehensively characterize both the tumor- and immune-related components of the tumor microenvironment while still retaining the ability to longitudinally monitor MRD and variants in the blood with industry-leading sensitivity, even in sample-limited scenarios.

Table 1

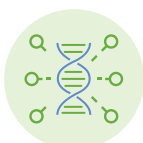
Key NeXT Personal Specifications		
General	Cancer Stage	All
	Cancer Type	Solid tumors
	cfDNA Input	15 ng
	Blood / Plasma Volume	10 mL (1 tube) / 4 mL
	Assay Type	Tumor-informed
	Front-End Tissue Sequencing	WGS
	Tissue Sequencing Coverage	>30X
	Plasma Sequencing	Targeted panel
	Plasma Sequencing Coverage	~100,000X (raw)
	Assay Multifunctionality	1. MRD 2. Tumor variant tracking 3. Customer-specified variant tracking
MRD	# MRD targets	1,800
	Analytical Sensitivity	1-3 PPM
	Analytical Specificity	≥99.9%
Tumor Variant Tracking	Variant capacity	400
	Source of variants	Coding regions only
	Analytical Sensitivity	0.1% VAF
Panel Variant Tracking	Variant capacity	1,000's
	Source of variants	Custom / Customer specified
	Analytical Sensitivity	0.1% VAF

Unique Features of NeXT Personal



Deep Sequencing

~100,000X raw coverage for plasma is performed across 1,800 loci, enabling sequencing dollars to be directed to variants of highest value. >30X WGS coverage for tumor and normal tissue is performed to detect SNVs for targeted panel inclusion.



Industry Leading MRD Performance

1-3 PPM MRD LOD is 10-100X more analytically sensitive than other MRD solutions on the market, aiding the detection of MRD and recurrence at the earliest timepoints. ≥99.9% specificity minimizes the rate of false positive results.



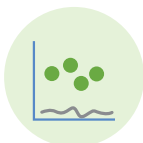
Assay Multifunctionality

NeXT Personal is not just an MRD solution: In addition to MRD, NeXT Personal tracks and annotates individual variants — those that are detected in the tumor, and those specified for panel inclusion by the user — to advance knowledge of tumor biology and observe emergence of known clinical and resistance hotspots.



Low Input Sample Requirements

NeXT Personal requires only 15ng of cfDNA, or 1 tube of blood (4mL of plasma), to deliver exceptional performance. Additionally, Personalis' protocols enable flexible sample formats — blood, plasma, and cfDNA — to be processed in the lab. Additionally, as little as 1mm³ of FFPE tumor tissue is required for WGS.



Advanced Error Suppression

Robust, proprietary error suppression techniques reduce the error rate from sequencing, PCR and other sample processing steps.



Panel Identification

Included in every NeXT Personal design, Personalis deploys a SNP-based quality control measure to ensure a patient's panel is never mixed with another patient's sample.



Personalis-Provided Panel Content

Personalis provides the option to include a carefully curated list of clinically actionable and resistance hotspots in addition to or in the absence of panel content specified by the user.

References

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4. Phylogenic tracking and minimal residual disease detection using ctDNA in early-stage NSCLC: A lung TRACERx study. Abbosh *et al.*, AACR 2020, Abstract CT023
5. Analytical development of the RaDaR™ assay, a highly sensitive and specific assay for the monitoring of minimal residual disease. Marsico *et al.*, AACR 2020, Poster 309
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7. Integrated digital error suppression for improved detection of circulating tumor DNA. Newman *et al.*, Nature Biotechnology, 2016.
8. Detection of circulating tumor DNA in early- and late-stage human malignancies. Bettegowda *et al.*, Science Translational Medicine, 2014.
9. Pan cancer analysis of whole genomes. Campbell *et al.*, Nature, 2020.





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DOC-001445(A)

EXHIBIT 2

EXHIBIT B

**IN THE UNITED STATES DISTRICT COURT
FOR THE DISTRICT OF COLORADO**

Civil Action No. 1:22-cv-01913-NRN

PERSONALIS, INC.

Plaintiff,

v.

FORESIGHT DIAGNOSTICS INC.

Defendant.

DECLARATION OF STEPHANE MOURADIAN, Ph.D.

I, Stephane Mouradian, declare:

1. I have personal knowledge of the following facts, or believe them to be true based upon information provided to me by others after a reasonable investigation. If called upon as a witness, I could testify to them competently under oath. This declaration includes facts known to me at the time of declaration. I reserve the right to supplement or amend in the future, including through testimony given at deposition or trial.

2. I have a Ph.D. in analytical chemistry, with a focus on DNA sequencing, from the University of Wisconsin at Madison.

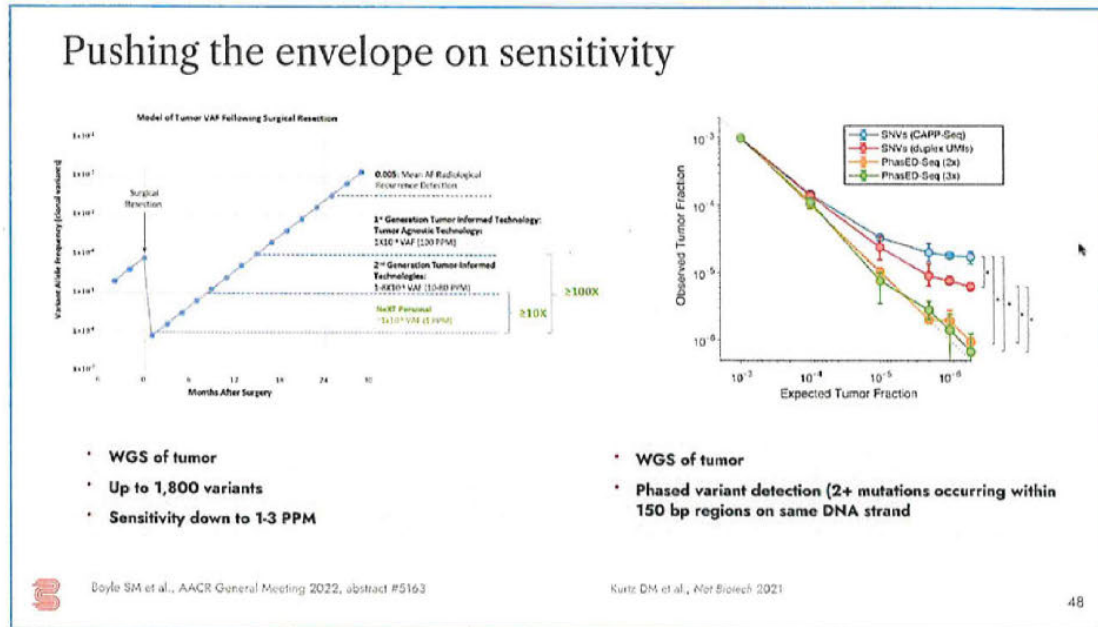
3. After completing my Ph.D. in 1996, I began working in the biotechnology industry and have over 25 years of industry experience. For roughly the first seven years of my career, I worked as a scientist both at 3M and then later at Caliper Life Sciences. In 2005, I transitioned to a business development role at Caliper, and in 2007 I moved to Perkin Elmer, where I was a Senior Director of Business Development. In 2012 I moved to Illumina, the largest worldwide provider of DNA sequencing products. Until 2018, I was a Director of Corporate and Business Development at Illumina. After spending a year in venture capital, I joined Personalis in 2019, where I am currently the Senior Vice President of Business Development and Marketing.

4. I have been informed that Foresight has challenged some of the patents at issue in the case with the Patent Office and is now seeking to halt this case pending resolution of these Patent Office challenges. I further understand that Foresight contends that Personalis would not be harmed if there were such a stay because there is supposedly no competition between Foresight and Personalis. For instance, I understand Foresight has stated that “Personalis cannot plausibly claim that it faces special or significant competition from Foresight” and that Foresight has pointed out that its testing product “is not approved by the FDA as an in vitro diagnostic, it is not CLIA validated (or validated by any other regulatory authority), and is not offered for sale to, or marketed to, patients or physicians.”

5. I disagree with Foresight’s assertions regarding the state of competition between Personalis and Foresight and whether Personalis would be harmed from a prolonged delay of this case. In fact, Personalis and Foresight are direct competitors, and Personalis would be harmed by a prolonged stay. Below, I explain why this is so.

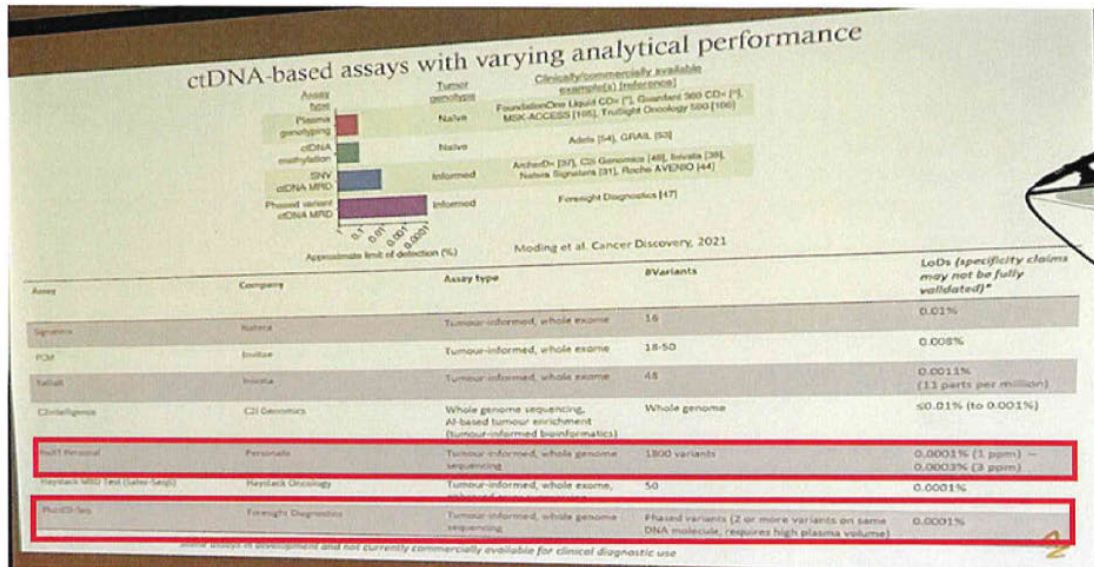
6. As background, both Foresight and Personalis offer testing products that can be used to monitor for cancer recurrence by detecting and analyzing tiny amounts of tumor DNA that are present in the bloodstream of a cancer patient. It is important to understand that both Foresight and Personalis offer testing products that operate according to the same basic principles, specifically, by using whole genome sequencing of a tumor sample to identify mutations that can subsequently be detected in circulating tumor DNA by capturing the mutation carrying DNA with capture probes and then sequencing the captured DNA. This unique approach distinguishes the Foresight and Personalis tests from other testing products, and allows the products from Foresight and Personalis to achieve greater sensitivity relative to other testing products currently on the market.

7. As such, industry groups and marketplace participants frequently compare the Foresight and Personalis tests side-by-side. For instance, BloodPAC, a consortium dedicated to accelerating the development of cancer testing assays based on analyzing blood samples, presented the following slide at a recent meeting:



On the left is an image showing the performance of the Personalis assay from a Personalis presentation and on the right is an image showing the performance of the Foresight assay from a Foresight publication. Notably, the title of the slide, “Pushing the envelope on sensitivity,” recognizes that Personalis and Foresight have assays that offer the highest sensitivity in the industry, which is a result of the fact that Foresight is using the same approach that is used in the patented Personalis assay. The main point, though, is that BloodPAC compared Personalis and Foresight side-by-side, which reflects that Personalis and Foresight offer directly competing products.

8. As another example, below is an image of a recent presentation prepared by [REDACTED] a major Personalis customer:



As the red boxes in the image shows, [REDACTED] is considering both the Personalis and Foresight assays together, and identifies them as both based on whole genome sequencing and as offering the same sensitivity levels. This again is a reflection of the fact that Personalis and Foresight are offering directly competing assays.

9. As noted above, I understand that Foresight has suggested that it does not compete with Personalis because the Foresight product “is not approved by the FDA as an in vitro diagnostic, it is not CLIA validated (or validated by any other regulatory authority), and is not offered for sale to, or marketed to, patients or physicians.” To the extent Foresight intends to suggest that there is no competition because the Personalis product is an in vitro diagnostic, CLIA validated, and/or marketed to patients or physicians, Foresight misunderstands how the Personalis assay is currently utilized in the market.

10. In fact, as of today, the Personalis assay, just like the Foresight assay, is not an in vitro diagnostic, CLIA validated, and/or marketed to patients or physicians. Rather, as of today, the

Personalis assay is utilized solely by pharmaceutical companies who are engaged in clinical trials that aim to test the efficacy of therapeutic drugs. This is precisely how the Foresight assay is used. In this regard, the Personalis and Foresight assays are not, as Foresight seems to suggest, serving different market segments, but actually serving the exact same market segments.

11. As confirmation of this, consider an advertisement feature that Foresight recently published in the journal *Nature*, which is one of the most highly-read and influential scientific journals. I have attached this advertisement as Exhibit A to my declaration. In the advertisement, Foresight emphasized the sensitivity of its assay, asserting that it has “developed a platform that detects circulating tumor DNA levels below one part-per-million.” Ex. A at 1. Foresight’s emphasis on sensitivity as a key feature underscores the direct competition between Foresight and Personalis.

12. What’s more, Foresight asserts in its advertisement feature that it “is seeking collaborations with clinical and pharmaceutical partners interested in exploring and jointly developing novel diagnostic and therapeutic strategies based on the enhanced MRD detection capabilities afforded by Foresight’s platform.” *Id.* In other words, Foresight is seeking to compete in the exact same market segment where Personalis currently sells all of its product.

13. Today, Personalis’ biggest customers include [REDACTED]

[REDACTED] Additionally, Personalis supplies testing services to a large number of smaller biotech companies. Based on our market intelligence, and Foresight’s advertisement feature, this is the exact same customer base as Foresight.

14. For instance, with respect to [REDACTED], which is one of Personalis’ most important customers, we regularly receive reports from our personnel in the field that Foresight is seeking to

capture business from [REDACTED] and we are currently facing direct competition from them. We understand that Foresight has an existing relationship with [REDACTED] related to blood cancer testing. Additionally, with respect to solid tumor testing products, we are currently engaged in what is commonly referred to in the industry as a “bake off” against Foresight in an effort to gain further business from [REDACTED]. Briefly, a “bake off” is a process whereby a potential customer compares two products side-by-side so as to make a decision regarding which product to use going forward.

15. [REDACTED] is a customer that potentially reflects tens of millions of dollars of revenue for Personalis, and the mere fact that Foresight is attempting to capture this business from [REDACTED] is damaging. Putting Personalis’ patent litigation lawsuit against Foresight on hold while Foresight’s Patent Office challenges proceed would give Foresight an expanded window during which it could attempt to capture not just this important business opportunity, but scores of other business opportunities. This, would, of course, cause great harm to Personalis.

16. Indeed, [REDACTED] is not the only customer where such concerns arise. Based on our market intelligence from Personalis personnel in the field, we understand that Foresight is engaging with at least the following additional Personalis customers: [REDACTED]
[REDACTED]

17. While Personalis is facing direct competition in the biopharma marketplace from Foresight, it is being harmed by Foresight’s presence in the marketplace in other ways as well.

18. For instance, both Personalis and Foresight attend the same industry meetings. Personalis has encountered Foresight, for instance, at the following major industry conferences: the American Association for Cancer Research meeting, the American Society of Clinical Oncology meeting,

the Society for Immunotherapy of Cancer meeting, and the Precision Medicine World Conference meeting.

19. At these meetings, both Personalis and Foresight are not only engaging with potential biopharmaceutical customers, but also key opinion leaders in academia that can be potential collaborators. This is a hugely important aspect of the ongoing competitive harm that we face from Foresight. Indeed, in order to further validate and test our testing product so that it can one day be used not only as a research tool but as a clinical product, we must have access to repositories of cancer samples for testing purposes. These repositories are most often generated and maintained by key opinion leaders in the field, such as major academic clinical researchers. We are regularly experiencing competition from Foresight in obtaining samples from these researchers.

20. As noted above, the Personalis assay is not yet a diagnostic clinical tool. But, our plan is to eventually be in this space, by first procuring CLIA accreditation and then eventually offering our test as a laboratory developed test to oncologists. We expect the same thing from Foresight, such that the scope of competitive harm we experience from Foresight will only continue to expand.

21. In this regard, it is also important to understand that the potential harm we are experiencing from Foresight is particularly acute given the nascent state of the market. I understand, for instance, that Foresight has submitted a declaration from Dr. Jacob Chabon, who is the CEO and founder of Foresight. In that declaration he states that “[t]oday, there are 18.1 million cancer survivors in the U.S. that could benefit from improved MRD testing, and according to the American Cancer Society that number is expected to grow to approximately 26 million individuals in 2040.” Dr. Chabon further states that he is “aware of more than 10 other companies, including

multi-billion dollar public companies, currently developing MRD diagnostic tests.” *Id.* In other words, the market for blood-based cancer testing products is at an inflection point, where researchers and companies have recently begun to recognize the great potential for blood-based testing technology.

22. As I explain above, the potential for Personalis to lose business to Foresight in this rapidly growing market is not mere speculation, but is something we are experiencing daily. Although, as Dr. Chabon notes, there are multiple other players seeking to offer blood-based cancer testing products, Personalis and Foresight are unique in their offering of tests based on the use of whole genome sequencing that provide substantially improved sensitivity relative to other products. This makes Personalis and Foresight unique head-to-head competitors. At this nascent stage in the market, if Personalis were to lose business to Foresight, it is possible that Personalis might never be able to recover that business and it is impossible to assess the scope of the resulting harm.

I declare under penalty of perjury under the laws of the United States that the foregoing is true and correct, and that this declaration was executed on December 20, 2022 in Fremont, California.

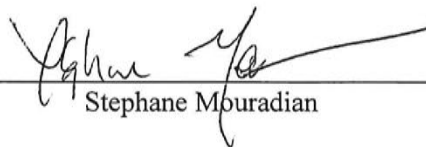
s/ 
Stéphane Mouradian

EXHIBIT A

Foresight Diagnostics
foresight-dx.com



Closing the gap on minimal residual disease detection in cancer

Foresight Diagnostics has developed a platform that detects circulating tumor DNA at levels below one part-per-million, allowing accurate identification of minimal residual disease well below current levels of detection. With testing available for B cell lymphomas and solid tumors, Foresight offers partnering opportunities ranging from investigational through prospective clinical studies and companion diagnostic development.

Current liquid biopsy assays are able to detect circulating tumor DNA (ctDNA) levels when tumor burden is high, but are not sensitive enough to detect minimal residual disease (MRD) when ctDNA levels are low. A significant portion of lymphoma patients eventually experience disease progression, and existing ctDNA assays fail to detect MRD in the majority of patients who will later relapse. Foresight Diagnostics, a privately-held cancer diagnostics company based in Aurora, Colorado, USA, has developed a novel liquid biopsy testing platform, PhasED-Seq, that allows detection of MRD with up to a 100-fold improvement in sensitivity over existing assays. Phased Variant Enrichment & Detection Sequencing (PhasED-Seq) detects ctDNA at levels below one part-per-million (<0.0001%) (ppm), a level of sensitivity that allows, for the first time, robust detection of ctDNA during and immediately after curative intent treatments across a variety of clinical settings (Fig. 1). One such application is the earlier detection of disease progression following curative intent treatment in patients with B cell lymphomas. PhasED-Seq provides an average gain of 200 days of lead time over existing disease surveillance platforms, which represents a fundamental shift in the ability to personalize treatment approaches for cancer patients and improve their overall survival prospects. The company is developing additional MRD assays based on PhasED-Seq technology for other tumor types, including a variety of solid tumors.

Potential applications of PhasED-Seq include the efficient development of new oncologic drugs, the design of new registrational pathways with MRD as an endpoint, and eventually the enhancement of clinical practice through MRD-guided treatment decisions.

"Despite the success of standard therapies in curing a large fraction of patients with B cell lymphomas, there is still a high unmet need for tools that can accurately and rapidly identify patients at risk of progression," said Jake Chabon, co-founder and CEO of Foresight. "Our ctDNA-based MRD detection platform, PhasED-Seq, provides a powerful new diagnostic tool for monitoring disease status during periods of low and previously undetectable tumor burden so that alternative treatments that could impact patient lives in very meaningful ways can be initiated as soon as possible."

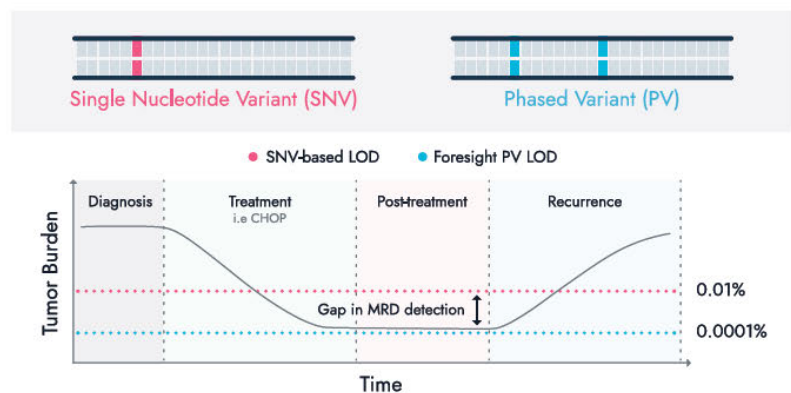


Fig. 1 | PhasED-Seq enables measurement of MRD at levels lower than SNV-based ctDNA detection. PhasED-Seq detects phased variants, ctDNA molecules harboring two or more SNVs, resulting in a 100-fold improvement in sensitivity over traditional SNV-based MRD detection platforms. This improvement in the limit of detection affords the possibility for continuous tumor detection both during and following treatment, thereby closing a critical gap in cancer management. ctDNA, circulating tumor DNA; LOD, limit of detection; MRD, minimal residual disease; SNV, single nucleotide variant.

Foresight is seeking collaborations with clinical and pharmaceutical partners interested in exploring and jointly developing novel diagnostic and therapeutic strategies based on the enhanced MRD detection capabilities afforded by Foresight's platform.

Zeroing in on MRD

A successful cancer treatment is defined by remission of the disease to undetectable levels. Unfortunately, the ability to determine whether remission is total and permanent is dictated by the ability to detect any traces of remaining disease, or MRD, that might seed a relapse. Over the past few decades the ability to detect MRD has rapidly evolved from radiographic determinations and histological analysis of solid biopsies to more sensitive and less invasive, liquid biopsy-based methodologies. Liquid biopsy refers to the analysis of bodily fluids, most commonly blood, to detect tumor-derived analytes such as circulating tumor cells (CTCs) or ctDNA.

The detection of ctDNA has shown great promise in helping identify MRD in several cancers, but the detection limits of the existing technologies still impose a 'treatment blind spot' of many months during which patients and their doctors must wait before making any decisions on potential follow-up treatment decisions.

Many existing ctDNA-based MRD approaches rely on detecting the minuscule fraction of tumor-specific single nucleotide variants (SNVs) present among the mostly non-cancerous freely circulating DNA contained in a liquid biopsy. The limit of detection (LOD) of a liquid biopsy platform thus rests on the ability to differentiate true, cancer-derived SNVs from non-tumor derived SNVs and potential sequencing errors in a large pool of background DNA.

Targeted sequencing techniques that track SNVs, such as cancer-personalized profiling by deep sequencing (CAPP-Seq) have improved the LOD of liquid biopsy approaches to approximately 100 ppm, depending on the approach. While these improved LODs have helped reduce the 'blind spot' following therapy when it is unclear whether a patient is cured, these approaches fail to detect MRD at the end of therapy in the majority of patients destined to relapse, delaying treatment decisions that could be lifesaving if implemented earlier.

"There are multiple milestones, including during therapy, at the end of therapy, and during the surveillance period after therapy, when physicians and patients could be making critical treatment decisions, but our inability to detect the exceedingly low MRD levels characteristic of those time points

prevents this from happening,” said Foresight co-founder and scientific advisor Ash Alizadeh, MD. “There is a need for new ways to track disease and therapy progression and improve individualized predictions and treatment recommendations.”

Improving the odds on ctDNA detection

Foresight has developed a new platform for MRD detection that decreases the LOD to tumor burden levels as low as 0.5 ppm, potentially eliminating treatment blind spots by enabling continuous MRD surveillance during and following therapy. This improved sensitivity for ctDNA detection is possible because of the implementation of PhasED-Seq, a new methodology recently developed by the cofounders of Foresight¹.

PhasED-Seq substantially improves the LOD for MRD detection by detecting two or more SNVs on individual DNA molecules. This approach overcomes the limitations of CAPP-Seq, which detects single SNVs on single DNA strands. The exponentially reduced probability of two or more SNVs being present on the same DNA strand as a result of co-occurring sequencing errors rather than true tumor-derived events results in a strong improvement in the signal-to-noise ratio and the resultant improved accuracy and performance of PhasED-Seq.

The key advance in Foresight’s approach is taking advantage of the fact that many SNVs are located within less than 170 base pairs from other SNVs. Given that the average size of a ctDNA fragment is ~170 base pairs, it’s possible to simultaneously identify two or more SNVs on the same DNA molecule. Such phased variants (PVs) are ubiquitous in cancers—some types of tumors such as B cell lymphomas are particularly enriched for PVs.

For the first implementation of its PhasED-Seq platform, the company focused on detecting MRD in liquid biopsy specimens from patients with B cell lymphomas. Specifically, the assay detects PVs in regions of the genome enriched for mutations arising due to the activation-induced cytidine deaminase (AID/AICDA) mutational process. These PVs are located in stereotypical areas of the genome and conserved across B cell malignancies, allowing for an off-the-shelf MRD solution that does not require patient-specific customization. In addition to PV-based MRD detection, Foresight’s MRD testing platform also provides comprehensive SNV and copy number variation genotyping that can be used for genetic subclassification and cell of origin determination in patients with diffuse large B cell lymphoma (DLBCL). The company has validated the clinical utility of the Foresight Lymphoma Assay in longitudinal clinical cohorts consisting of 678 specimens from 213 patients with DLBCL. In a recent publication¹, MRD detection using Foresight’s PhasED-Seq platform was directly compared to SNV-based ctDNA detection both during and following two cycles of immunochemotherapy. During treatment, the assay correctly detected 88% of patients in need of additional therapy versus only a 46% correct detection rate with the SNV-based ctDNA approach. Post-treatment, the success rate for the assay went up to 100% compared to 40% for SNV-based ctDNA detection (Fig. 2).

A PhasED approach to solid tumors

Foresight’s research has revealed that while solid tumors also contain PVs, these tend to be more

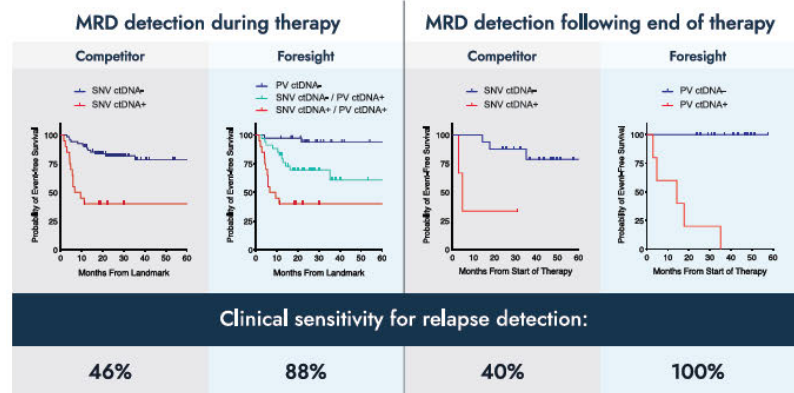


Fig. 2 | PhasED-Seq MRD testing improves clinical outcome stratification. In clinical studies, PhasED-Seq improves MRD detection both during treatment and immediately following treatment compared to SNV-based approaches¹. During treatment, PhasED-Seq improved recurrence prediction by approximately two-fold; following treatment (left); PhasED-Seq improved recurrence prediction from 40% to 100% (right). MRD, minimal residual disease; SNV, single nucleotide variant.

broadly distributed across the genome. To take advantage of the improved detection sensitivity and specificity of PhasED-Seq with solid tumors, Foresight generates panels of patient-specific PVs.

In a pilot study of five patients with lung cancer and one with breast cancer, PhasED-Seq was 62.5% successful in detecting potential relapse versus only 37.5% with an SNV-based ctDNA assay. Importantly, the sensitivity achieved with PhasED-Seq in solid tumors—down to 1 ppm—is equivalent to those achieved with B cell lymphomas. While the implementation of PhasED-Seq for MRD detection in solid tumors requires obtaining biopsy samples from individual patients, the potential for making treatment decisions significantly earlier due to the much lower LOD afforded by PhasED-Seq provides the Foresight platform with a clear advantage for patients. Foresight projects that its MRD technology will be applicable to the majority of solid tumors including breast, lung, colorectal, liver, kidney, uterus, skin, and pancreatic cancers.

“Foresight’s MRD detection platform has the potential to impact disease management in unprecedented ways, both for blood cancers and solid tumors,” said Chabon. “A reliable negative test would help with making a decision about withholding potentially toxic and expensive additional treatment, and conversely, a highly sensitive positive test would provide actionable data to plan follow-up treatment while the disease burden is still low and patients are more likely to respond.”

MRD detection with real-time Foresight—a continuum of opportunities

The high sensitivity of Foresight’s MRD assay provides, for the first time, the possibility to monitor MRD and the potential for relapse detection in real-time and with high accuracy, opening the door to a bevy of opportunities both in drug development and clinical settings. These encompass efficient development of new oncologic drugs, including new registrational pathways with MRD as an endpoint, and potentially changing clinical practice through MRD-guided treatment decisions. Specifically, a number of immediate clinical trial scenarios in which implementation of the PhasED-Seq-based MRD detection platform would be highly beneficial can be envisioned.

- **Risk-adapted randomized trial design.** Assessment of MRD after only one to two cycles of R-CHOP treatment (rituximab-cyclophosphamide, doxorubicin hydrochloride, vincristine [Oncovin], prednisone) in B cell non-Hodgkin lymphoma would allow for early identification of patients who are not responding to therapy and are in need of additional treatment.
 - **Increased trial size.** The improved clinical sensitivity of the Foresight MRD assay could allow for higher patient enrollment rates due to better screening capability.
 - **Reduced trial costs.** Improved screening sensitivity would reduce time and costs to identify the necessary number of registrants for a trial.
 - **MRD as surrogate trial endpoint.** Higher sensitivity of the MRD test could provide a clinically appropriate endpoint for treatment, allowing trial completion sooner than with existing endpoints such as progression-free survival at 24 months.
- To cover the range of possibilities from investigational studies to clinical trials and companion diagnostic development, Foresight is actively building out its operational infrastructure and testing capabilities at the company’s US Clinical Laboratory Improvement Amendments (CLIA)-registered laboratories, where it offers research-use-only and CLIA-certified testing options for researchers and clinicians.

“Foresight’s MRD detection platform can, for the first time, provide actionable real-time information to physicians and biopharmaceutical companies to enable more personalized treatment approaches for patients with cancer,” said Mukul Agarwal, CFO and CBO of Foresight. “We believe our platform will become the future standard of care for MRD detection, and we are looking to partner with others on turning this potential into a reality for cancer patients worldwide.”

1. Kurtz, D.M. et al. *Nat. Biotechnol.* 39, 1537–1547 (2021).

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EXHIBIT 3

Analytical performance of an ultra-sensitive, tumor-informed liquid biopsy platform for molecular residual disease detection and clinical guidance

#3381

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BACKGROUND

Early detection of cancer recurrence and treatment monitoring using non-invasive procedures such as circulating tumor DNA (ctDNA) profiling is an emerging new strategy for cancer patient care. ctDNA is shed by primary or metastatic tumor cells and contains tumor-specific somatic mutation signatures. However, most ctDNA-based molecular residual disease (MRD) detection methods leverage a limited genomic footprint, restricting detection sensitivity to 10⁻⁴ ~ 10⁻⁵ tumor fraction and thus their utility in many clinical settings^{1, 2}. In the post-diagnosis situation, early detection of cancer, especially those with low tumor mutational burden (TMB)³, may become challenging if they do not harbor sufficient variants in these limited footprints to produce detectable signals. Further, insights into tumor evolution, including actionable mutations may be missed.

Here we report a performance update of the NeXT Personal® platform. NeXT Personal utilizes hybridization-capture-based technology to quantify ctDNA in liquid biopsy samples. Its unified probe panel design and workflow simultaneously detects and monitors MRD, surveys known cancer-related clinical variants, and quantifies and tracks investigational variants of interest, by leveraging both tumor-informed and tumor-agnostic genomic information (Fig. 1). The tumor-informed MRD content is dedicated to personalized MRD detection and longitudinal monitoring, which utilizes cumulative tumor-derived signals to achieve ultra-high sensitivity down to 1 ~ 3 parts per million (PPM) limit of detection (LOD). The tumor-agnostic clinically relevant content surveys known and validated actionable genomic variants in 90 clinically relevant genes, and serves to inform therapy selection and detect existing or potentially emerging events such as new subclones or metastases. The investigational content provides capacity to track important cancer-related variants for research or investigational purposes.

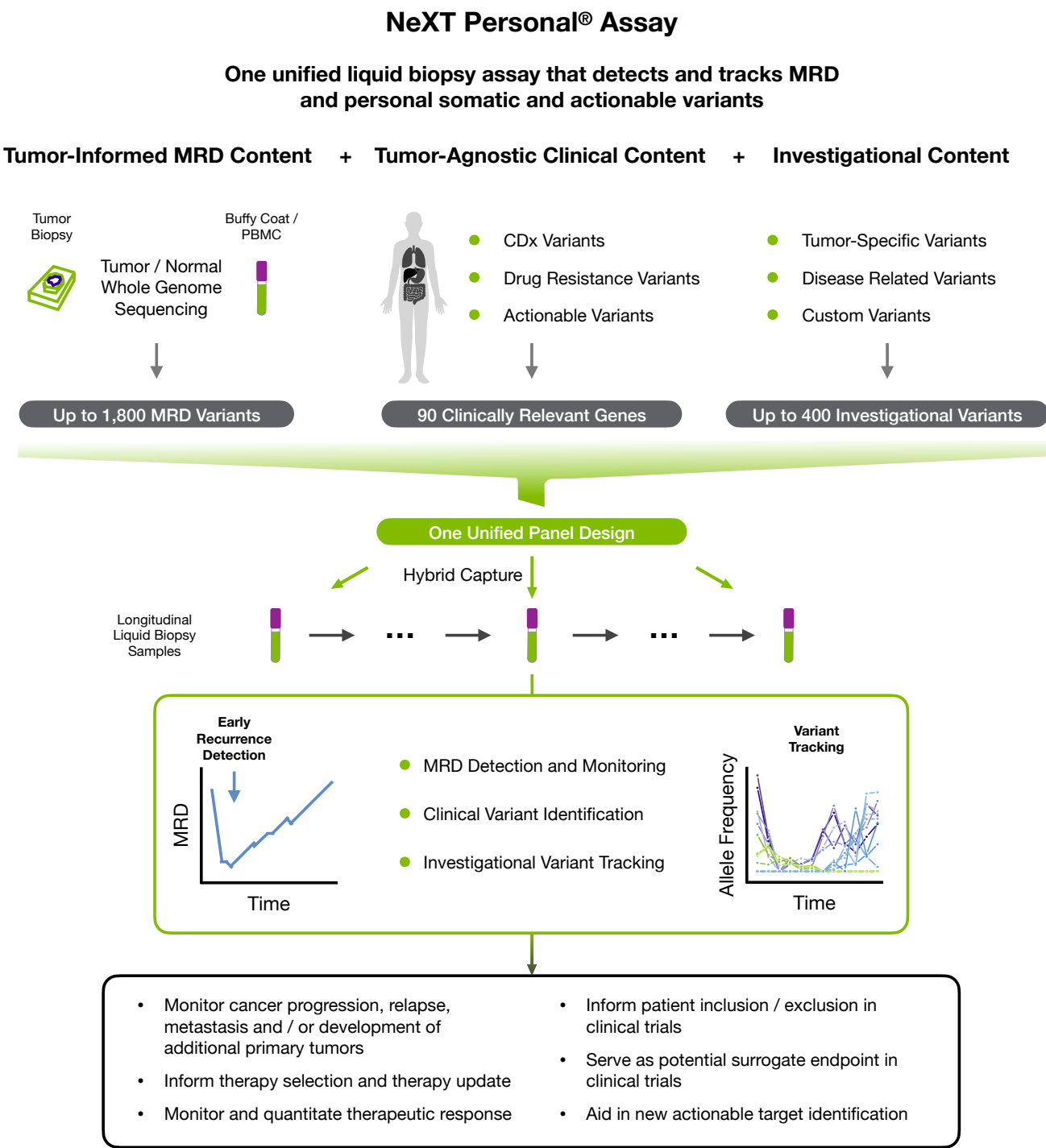


Figure 1: NeXT Personal Assay Overview.

References:
1. Odegaard, J. I. et al. *Clin Cancer Res.* 24, 3539–3549 (2018).
2. Reinert, T. et al. *JAMA Oncol.* 5, 1124–1131 (2019).
3. Merino, D. et al. *J Immunother Cancer.* 8, e000147 (2020).

METHODS

The NeXT Personal assay requires a single tube of peripheral blood (1 ~ 8 mL plasma or 2 ~ 50 ng cfDNA) for each monitoring time point, as well as 1 upfront tumor biopsy sample (fresh frozen or formalin-fixed paraffin-embedded sections, 1 mm³ in size) paired with a matched normal sample (e.g. buffy coat or peripheral blood mononuclear cells) to identify tumor-specific genomic content. All experiments were performed in the Clinical Laboratory Improvement Amendments-certified and College of American Pathologists-accredited laboratories at Personalis, Inc. following standard operating procedures. The tumor-informed MRD content (up to 1,800 variants) and Investigational content (up to 400 variants) for each panel were designed by identifying high quality and low noise tumor-specific genomic variants based on matched tumor-normal whole genome sequencing using proprietary algorithms. The tumor-agnostic clinically relevant content was predesigned for all panels (subject to periodic review and update), which surveys known and validated actionable genomic variants such as companion diagnostic (CDx) variants, drug resistance hotspots and other actionable variants in 90 clinically relevant genes. Data analysis was performed using the proprietary production analysis pipeline for NeXT Personal.

RESULTS

Analytical Performance of MRD Detection

In a series of 75 cfDNA samples with artificially constructed tumor fractions (TF) ranging from 10⁻⁶ to 5 x 10⁻¹, the assay detected signals as low as 1.95 PPM (Fig. 2, p-value < 1 x 10⁻⁴). The median LOD was 1.45 PPM (range: 1.17 - 1.69 PPM). Our results showed a very high linear correlation (Pearson R² = 0.999) between observed and expected MRD signals that span over 5 orders of magnitude. The detected MRD signals were also orthogonally confirmed by ddPCR (Fig. 3, Pearson R² = 0.917, PPA = 100%, NPA = 100%). Note the high linear correlation between the NeXT Personal MRD signals and the tumor signals detected by ddPCR, and that NeXT Personal detects signals 100 ~ 1000X lower than ddPCR's LOD (solid circles, actual ddPCR readings; hollow circles, imputed ddPCR readings from higher concentration measurements due to ddPCR's LOD). In addition to the ultra high sensitivity, high MRD detection specificity (100% observed, 95% CI: 98.22-100%) was also demonstrated by assaying 205 patient-specific panels (representing 12 distinct tumor types) on unrelated healthy donors who are expect to display no signal at any target loci (Table).

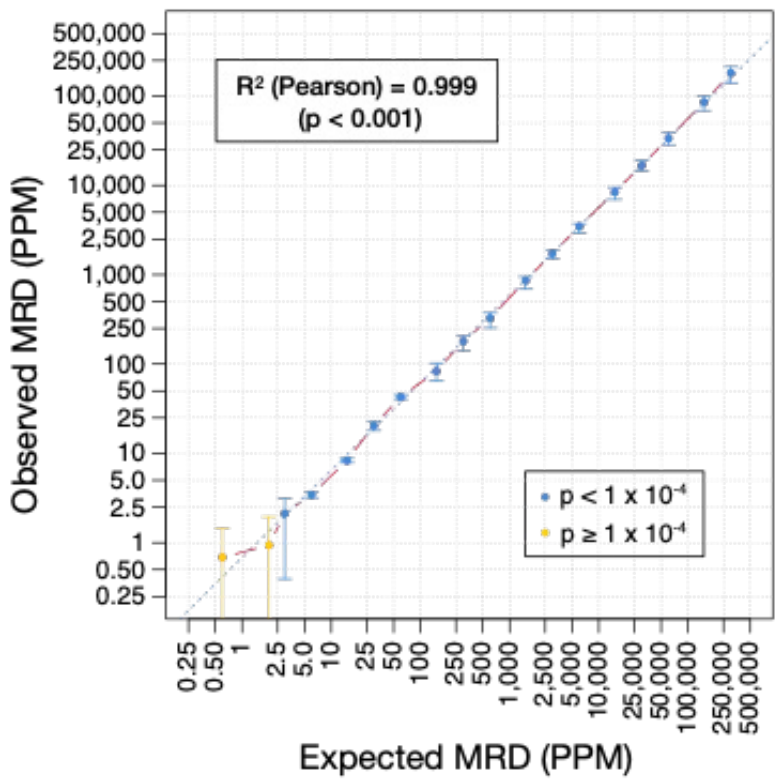


Figure 2: MRD Detection Sensitivity.

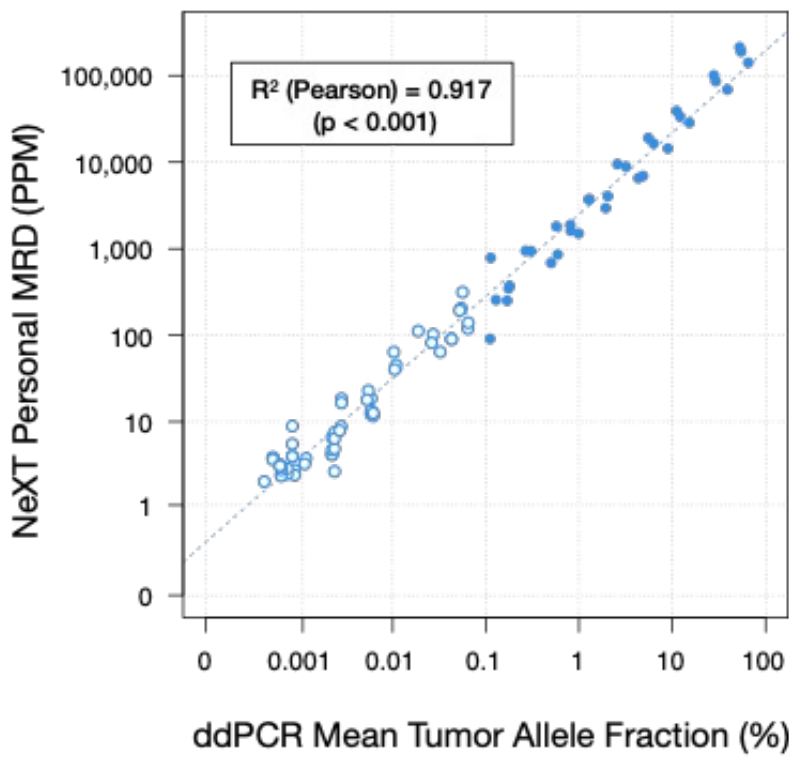


Figure 3: ddPCR Confirmation of MRD Signals.

Number of Patient-Specific Panels	True Negative MRD Detections	False Positive MRD Detections	Specificity
205	205	0	100% (95% CI: 98.22-100%)

Analytical Performance of Genomic Variant Tracking

The NeXT Personal assay reports individual genomic variant detection with VAF ≥ 0.1% (recommended p-value threshold < 1 x 10⁻⁶). High detection PPV, NPV, sensitivity, specificity and overall accuracy were observed in all VAF ranges, with high measurement precision shown by observed / expected VAF ratios (Fig. 4). In addition, VAF measurement precision and signal linearity was orthogonally confirmed by ddPCR for 17 clinical variants (Fig. 5), showing 100% agreement (Cohen's κ = 1.00).

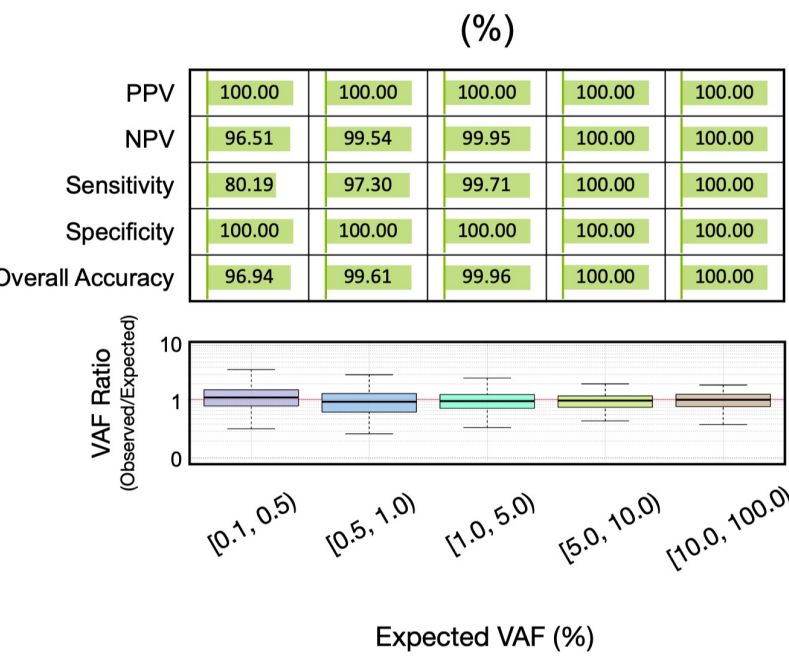


Figure 4: Variant Detection Performance.

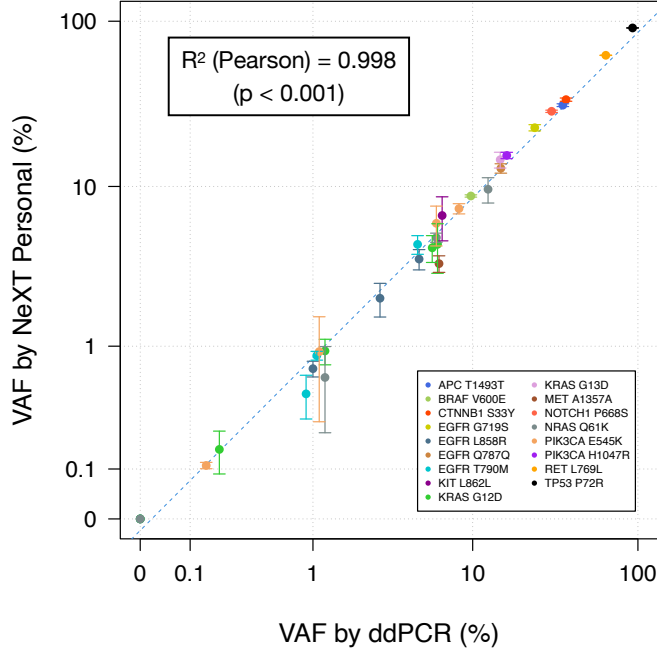


Figure 5: ddPCR Confirmation of VAF Calls.

Clinical Applications

A retrospective analysis was undertaken in an advanced liver cancer (low TMB) cohort of 11 patients undergoing immunotherapy. ctDNA levels in longitudinal plasma samples were measured with NeXT Personal. Our results (Fig. 6) demonstrated that changes in ctDNA levels during therapy correlated highly with disease status [patients with progressive disease (PD) vs. patients with disease control i.e. partial response (PR), complete response (CR) or stable disease (SD): 3wk to baseline % change, Wilcoxon signed rank test (one-sided) p = 0.026; 6wk to baseline % change, p = 0.011; 9wk to baseline % change, p = 0.0022], and were detected prior to clinical response confirmation by RECIST 1.1.

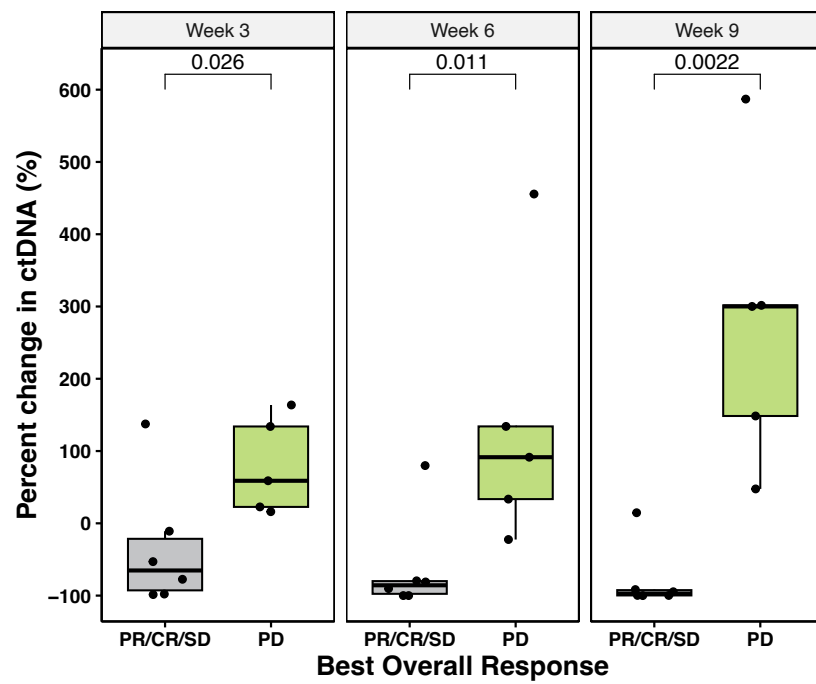


Figure 6: ctDNA Change Observed During Immunotherapy.

CONCLUSION

In summary, we present the analytical performance of NeXT Personal, a highly sensitive and specific personalized liquid biopsy assay for MRD and individual clinical and investigational mutation detection and monitoring. With verified LOD of 1 ~ 3 PPM for MRD and 0.1% VAF for individual mutations, our assay is sufficiently sensitive for residual or recurrent cancer detection in even challenging situations such as early stage, low shedding, or low TMB cancers, at earliest possible time points with low input cell-free DNA amount required. Moreover, the demonstrated high assay specificity and signal linearity ensures that the detected signals are true and accurate measurements of the residual disease. Mutation level information from 90 clinical genes also helps identify actionable targets and informs therapy selection and therapy update. The assay benefits from both tumor-informed and tumor-agnostic genomic information, making NeXT Personal unique in its capability to detect and monitor MRD while informing and guiding clinical decisions.