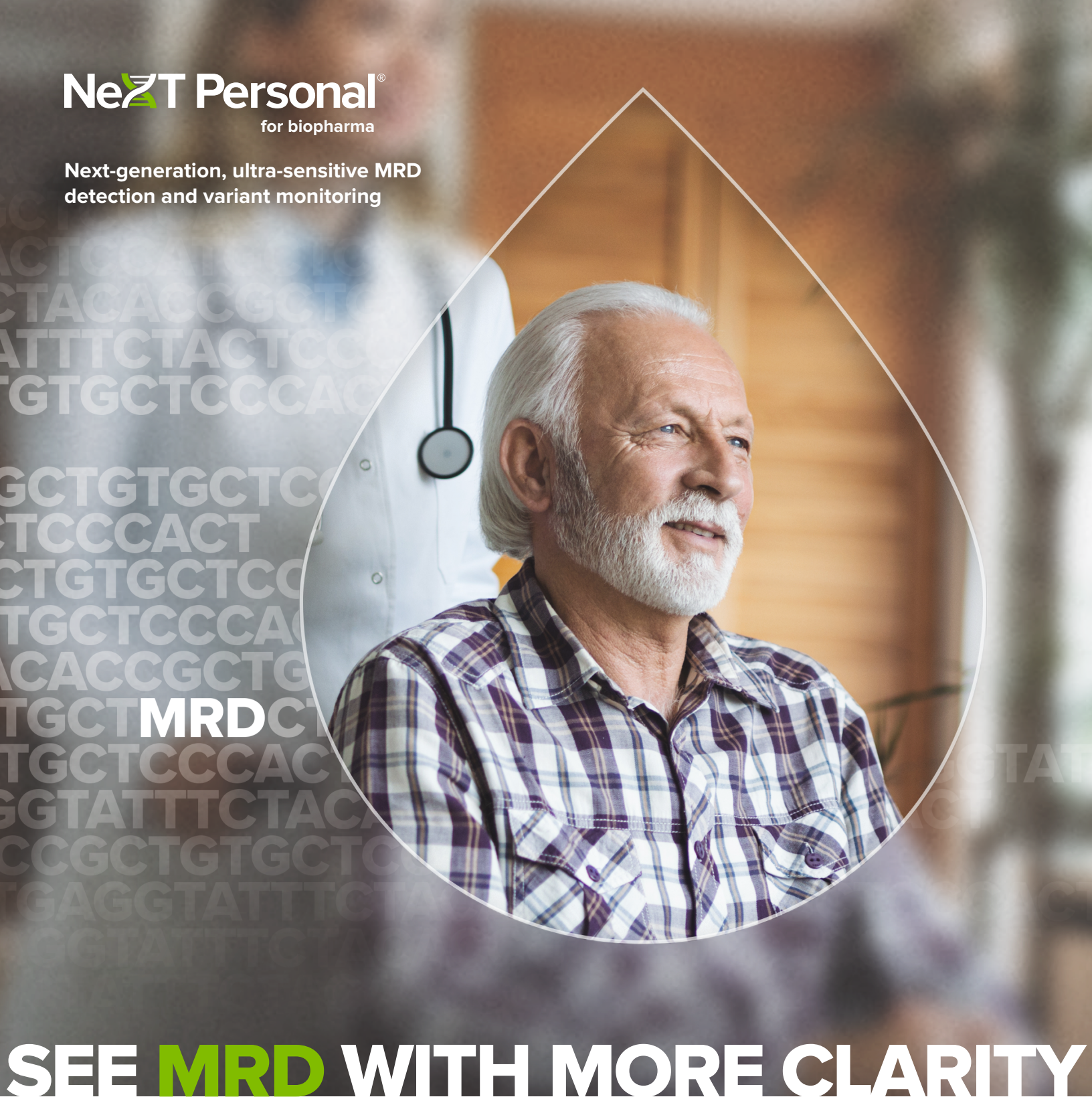
NeXT Personal®
for biopharma

Next-generation, ultra-sensitive MRD detection and variant monitoring



SEE MRD WITH MORE CLARITY

What would it mean for your clinical trials if you could detect tumor burden at ultra-low levels?

Personalis®

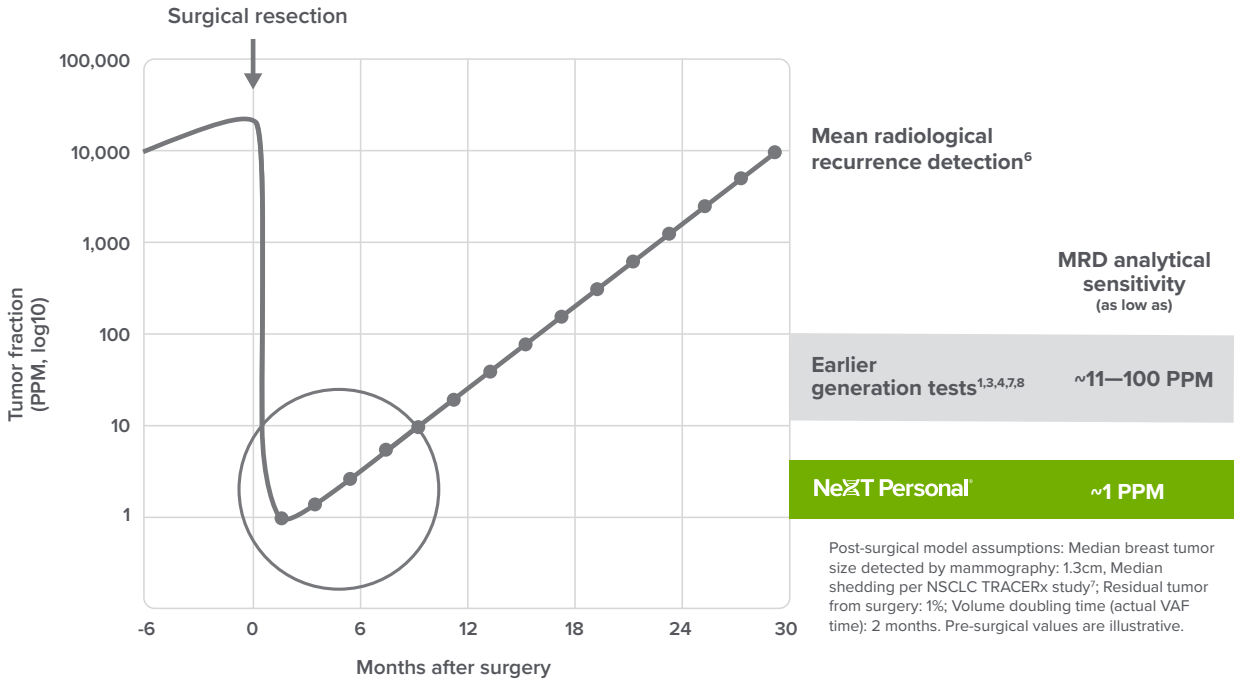
MRD sensitivity matters

Discover next-generation molecular residual disease (MRD) detection

The need for sensitive MRD detection

MRD is rapidly emerging as a key biomarker in cancer therapy development. However, achieving reliable, sensitive detection and quantification of MRD remains a challenge for current technologies that use circulating tumor DNA (ctDNA), particularly in early cancer stages. NeXT Personal® is the world's most advanced tumor-informed liquid biopsy assay. It delivers 10–100X more MRD analytical sensitivity than other available methods[1–5], without sacrificing analytical specificity, allowing you to detect evidence of cancer much earlier than other technologies.

Figure 1. Model of tumor fraction following surgical resection



Maximize your study

Empower your drug's success

Key benefits for clinical trials

Accurately quantifying MRD at the earliest timepoints can empower successful clinical trials and accelerate the development of new therapies. On one hand, standard of care (SOC) imaging-based technologies remain limited in their ability to detect low tumor volume.[6] On the other hand, many ctDNA technologies and detection thresholds vary widely. This impacts their sensitivity, how early they can detect MRD, and how reliably they can assess treatment efficacy. NeXT Personal® achieves more sensitive detection and quantification of MRD. Our proprietary tests and algorithms can enhance clinical trial success through:

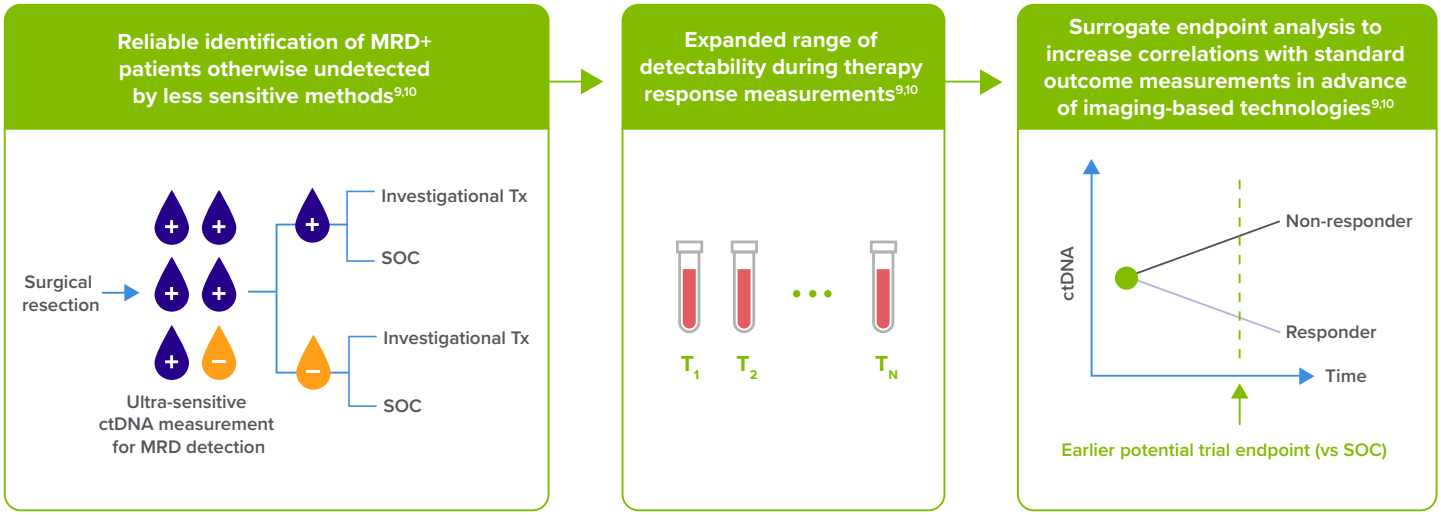
Increased accuracy of patient stratification for efficient enrollment

Reduced trial time and cost by finding MRD-positive (MRD+) patients faster

Shorter time to surrogate endpoint analysis through earlier detection of MRD

Enhanced ability to measure therapy response, both immediate and durable

Figure 2. How NeXT Personal® empowers your clinical trials



MRD+: MRD-positive | Tx: therapy | SOC: standard of care

Powerful technology that delivers reliable answers

Personalis is pioneering blood-based cancer detection and monitoring to unlock unprecedented sensitivity and specificity at the same time, while offering rich longitudinal tumor insights. NeXT Personal® offers:

Ultra-sensitivity you can trust

Reduces false negative rates with its analytical sensitivity that is up to 100X superior to other MRD tests

Uncompromised ultra-high specificity[11]

Reduces false positive detection, powered by our proprietary NeXT SENSE™ technology

Unmatched insights

Uncovers and tracks driver and resistance mutations simultaneously with MRD detection in a single assay

Broad inputs and applications

Allows you to work with a multitude of challenging samples types, including low-input samples

Clinical trial assay & regulatory pathways for trial enrollment/patient stratification:

- Laboratory Developed Test (LDT) availability for earlier phase studies
- Ability to partner to develop a clinical trial assay for later phase studies
- Commitment to partner on CDx development
- Regulatory support throughout
- Infrastructure and sales footprint for commercialization

One assay. Multiple functions. Deeper understanding.

Access richer insights with a new approach to ctDNA detection and tracking

Combine NeXT Personal® MRD and variant tracking under one platform to get deep insights into low tumor signal, and uncover underlying mechanisms of therapy response.

Figure 3: The NeXT Personal Assay

+

Core

Quantitative MRD detection

Does the patient have molecular evidence of cancer? Is the patient responding to therapy?

- Industry-leading 1 PPM ($1x10^{-6}$) analytical sensitivity
- Low noise to enable ≥99.98% specificity[11]
- MRD status (+/-) and quantitative tumor fraction measurement

Add-on

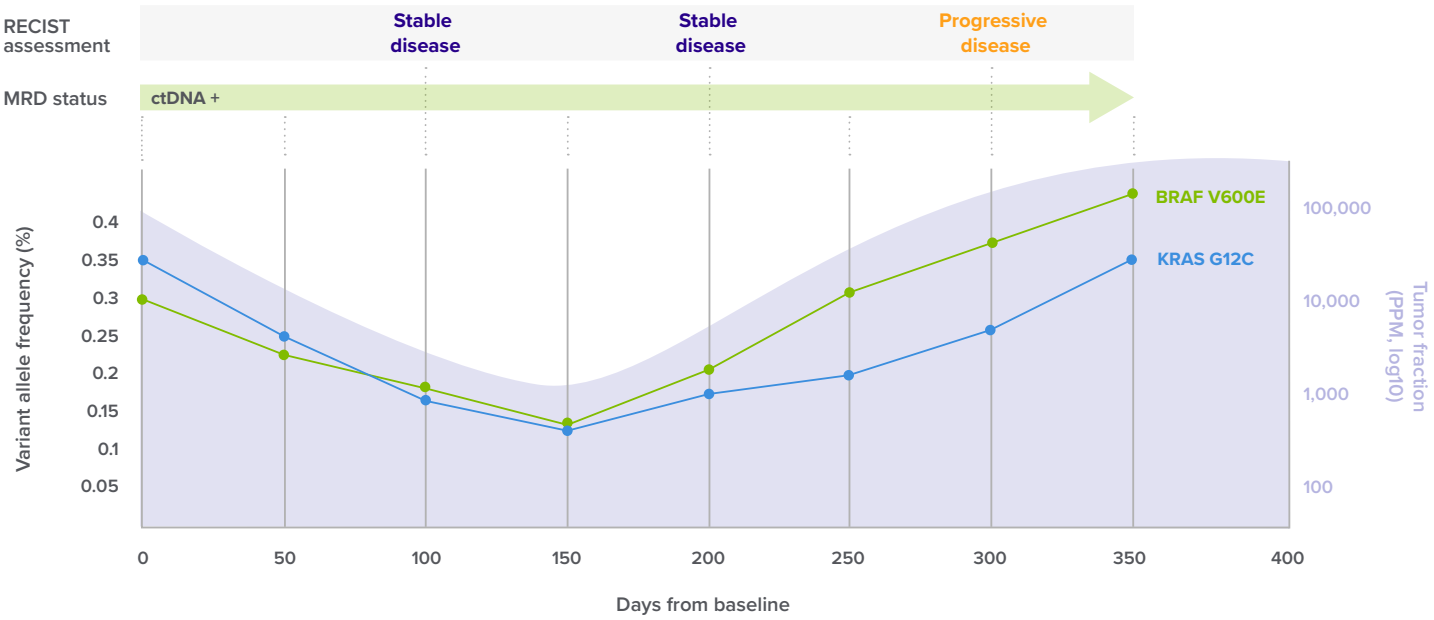
Optional add-on variant tracking

What are the mechanisms underlying treatment response?

- Option 1: Pre-defined driver and resistance mutation tracking
- Option 2: Tumor-informed variant tracking
- Option 3: Custom variant tracking (e.g. neoantigens)

By offering the option to simultaneously detect and monitor clinically-relevant variants with MRD, NeXT Personal® provides a new level of insight into cancer evolution beyond tumor fraction alone. This assay can also incorporate custom targets of interest such as personalized neoantigens to help you evaluate how a tumor responds to therapy.

Figure 4. Response monitoring using tumor fraction and variant detection analysis

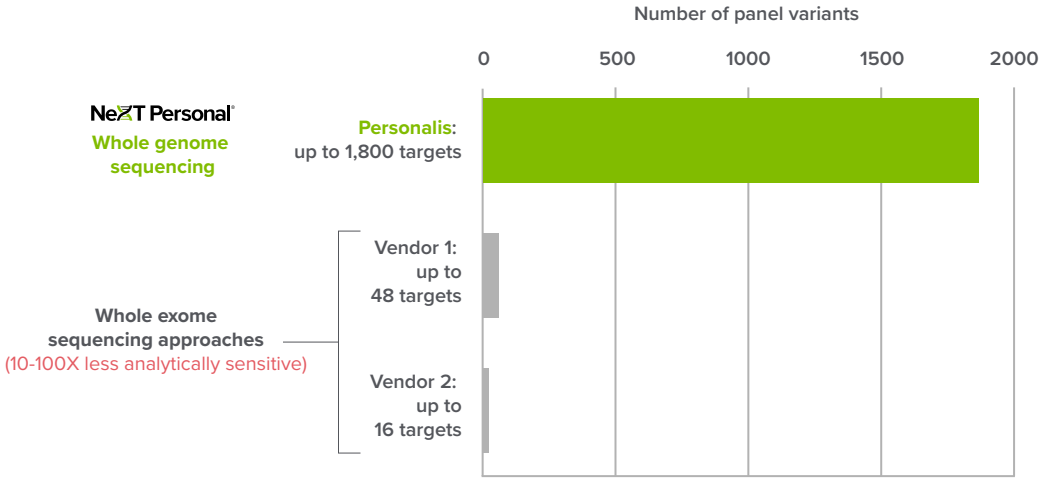


The power of a genome-wide approach

Harness the benefits of industry-leading target breadth

Narrower tumor-informed panel footprints (i.e. those using tissue-based exome sequencing, or tumor-agnostic panels that do not leverage the tumor signature from tissue sequencing), may not be sufficient to detect MRD at low tumor fractions or under challenging conditions.

Figure 5. Number of variants targeted by NeXT Personal® vs whole exome sequencing approaches



1,800 tumor-derived mutations (SNVs*) detected, mostly in non-coding regions. NeXT Personal® selects mutations that are most likely to be shed into the blood and have high signal-to-noise profiles.
*Single Nucleotide Variant

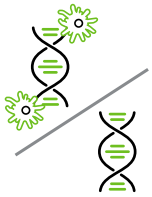
Leveraging WGS as the front end tissue assay, NeXT Personal® achieves higher sensitivity by:

- Targeting more variants than other approaches
- Targeting variants of higher quality that are not always found in coding regions, using
  - Higher allele frequency
  - Higher signal-to-noise ratio
- Applying advanced noise suppression in plasma

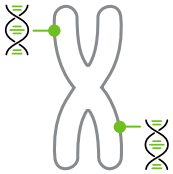
Overcome challenging sample conditions

While leveraging tissue WGS enables ultra MRD sensitivity through the identification and inclusion of up to 1,800 variants in the panel, it also enables the ability to mitigate challenging sample conditions, frequently due to:

Low plasma volume



Low tumor fraction/poor shedding[12]



Highly variable tissue TMB[13]

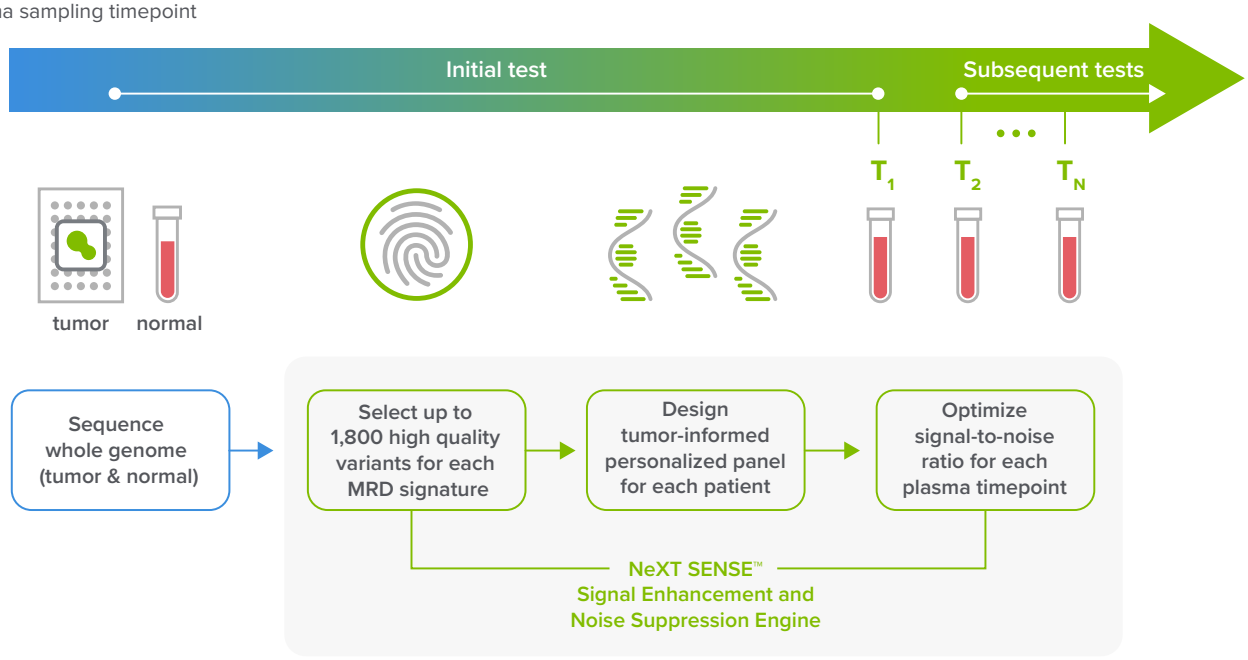
Unlock high-fidelity tumor signal with our proprietary noise reduction technology

Create patient-specific panels

As a tumor-informed approach, NeXT Personal® builds patient-specific panels based on a broad, comprehensive, WGS-derived tumor signature. Our proprietary NeXT SENSE™ (**S**ignal **E**nhancement and **N**oise **S**uppression **E**ngine) technology is leveraged across the workflow to reduce the error rate from sequencing, and other processing steps.

Figure 6. Creating a unique cancer test for each patient is key to sensitive ctDNA detection and tracking

T = Plasma sampling timepoint



Personalis is the first company to develop patient-specific panels leveraging tissue WGS.

Leverage the power of NeXT SENSE™ noise suppression technology

MRD false positives may confound study analysis. This can lead to the wrong patients being enrolled, as well as unreliable longitudinal detection. To ensure data reliability, it is crucial to use MRD assays that do not compromise specificity to reach ultra-high sensitivity. Optimized for both sensitivity and specificity and powered by NeXT SENSE™ technology, NeXT Personal® ensures exceptionally low false-positive ctDNA detection, through:

- Advanced, proprietary statistical analyses distinguishing signal from noise for each individual patient panel and sample
- Enrichment of low-noise, locus-specific tumor signal
- Stringent p-value threshold of ≤0.001 derived from a specificity target of ≥99.9%[11] for making MRD calls

Our specificity studies[11] have demonstrated robust performance when cancer panels were used to sequence healthy donor plasma samples, and an extensive alternative design in silico verification.

Figure 7. The NeXT Personal® MRD assay delivers ultra-specificity[11]

Specificity analysis	# Panels	# False positives	Observed specificity	Lower 95% CI	Upper 95% CI
Empirical	205	0	100%	98.22%	100%
Alternative design analysis*	40,600	7	99.98%	99.96%	99.99%

* extrapolation

Maximize insights from small samples

NeXT Personal® delivers unparalleled performance even with small samples. In addition, Personalis' protocols enable flexible and minimally invasive sample formats—blood, plasma, and cfDNA—to be processed in the lab.

As little as 1mm^3 of FFPE tumor tissue required for WGS

Only 4mL of plasma (2–8mL range) or 15ng of cfDNA (range 2–30ng)

A powerful combined solution

Discover an all-in-one platform for a multidimensional view into tumor biology

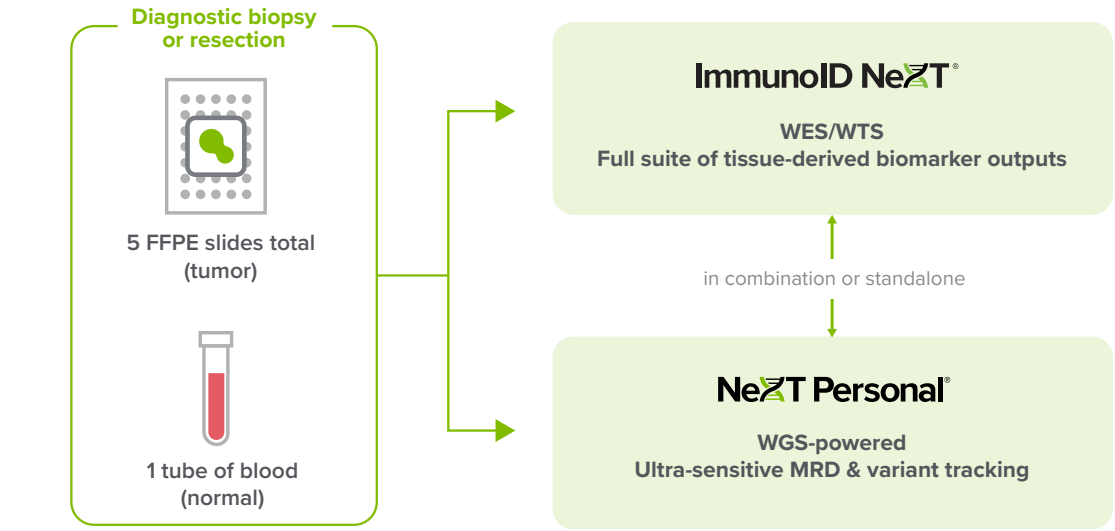
ImmunoID NeXT® is an ultra-comprehensive biomarker discovery platform that interrogates the complex interactions between a tumor and its microenvironment. This powerful platform also provides visibility to genomic features that might otherwise be missed.

Minimal input material from a single sample. Maximal data from each sample.

Investigators can run both ImmunoID NeXT® and NeXT Personal® from the same sample, unlocking the ability to:

- Comprehensively characterize both the tumor- and immune-related components of the tumor microenvironment
- Longitudinally monitor MRD and variants with high sensitivity, even in sample-limited scenarios

Figure 8: Tumor profiling and ultra-sensitive detection



Two plasma tubes required for serial monitoring

NeXT Personal technical specifications

Get to know NeXT Personal

Table 1. Performance specifications and features

General	Cancer stage	All
	Cancer type	Solid tumors
	cfDNA input	15ng target; range 2–30ng
	Blood / plasma volume	4ml target; range 2–8ml
	Assay type	Tumor-informed (MRD)
	Front-end tissue sequencing	WGS
	Tissue sequencing coverage	>30X
	Plasma sequencing	Targeted panel
	Plasma sequencing coverage	Up to ~100,000X (raw)
	Assay multifunctionality	1. MRD 2. Optional add-on content module
MRD	#MRD targets	Up to 1,800
	Analytical sensitivity	1–3 PPM LOD
	Analytical specificity	≥99.98%
Optional add-on variant tracking	Variant capacity	Up to 400 unique loci
	Sources of variants	Option 1: Pre-defined driver and resistance mutations Option 2: Tumor-informed variant tracking Option 3: Custom variant tracking (e.g. neoantigens)
	Analytical sensitivity	0.1% VAF LOD

1. Sethi, H. *et al. Abstr. 4542* (2018) **2.** Nordentoft, I. *et al. J. Clin. Oncol.* 39, e16527–e16527 (2021) **3.** Abbosh *et al., AACR, Nature* (2023) **4.** Marsico, G. *et al. in Cancer Research, AACR* - poster #3097 80, 3097 (2020) **5.** Internal data on file. **6.** Adler, S. *et al. EJNMMI Phys.* 4, 13 (2017) **7.** Abbosh *et al., AACR, Nature* (2017) **8.** Zhao, J. *et al. Mol Diagn Ther* (2023) **9.** FDA Draft Guidance. May 2022 (Source: https://www.fda.gov/media/158072/download) **10.** Vellanki PJ *et al. R,* 2023:11:e005344. doi: 10.1136/jitc-2022-005344 **11.** Personalis specificity study. (2023) **12.** Bettegowda, C. *et al. Sci. Transl. Med.* 6, 224ra24 (2014) **13.** Alexandrov, L. B. *et al. Nature* 500, 415-421 (2013)

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