Biofidelity.

ASPYRE Technology

Breaking down the barriers to optimized therapy for all.

ASPYRE®

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Breaking Down Barriers to Biomarker Testing

In the past two decades, significant advances in DNA sequencing have transformed our understanding of the molecular pathways that drive many cancers and led to the development of highly effective targeted therapies that offer patients better outcomes, fewer side effects and improved quality of life.

Guidelines from the National Comprehensive Cancer Network (NCCN) recommend that most cancer patients diagnosed with Stage IV cancer be tested to identify any genomic alterations that could be successfully managed with targeted therapeutics.

Unfortunately, advances in precision oncology treatments have outpaced current molecular testing technologies, which have significant limitations that prevent widespread adoption. As a result, fewer than 50% of patients diagnosed with cancer actually undergo the biomarker testing needed to accurately guide their treatment.

Fact

Fewer than 50% of cancer patients who could benefit from targeted therapy actually undergo the biomarker testing needed to accurately guide their treatment.

Selecting the best treatment option requires a molecular diagnostic test to identify mutations, or biomarkers, associated with targeted therapies.

> "ASPYRE was designed to break down the barriers to comprehensive biomarker testing and ensure that all patients have access to the best treatment options."

Limitations of Current Biomarker Technologies

Preventing Widespread Adoption

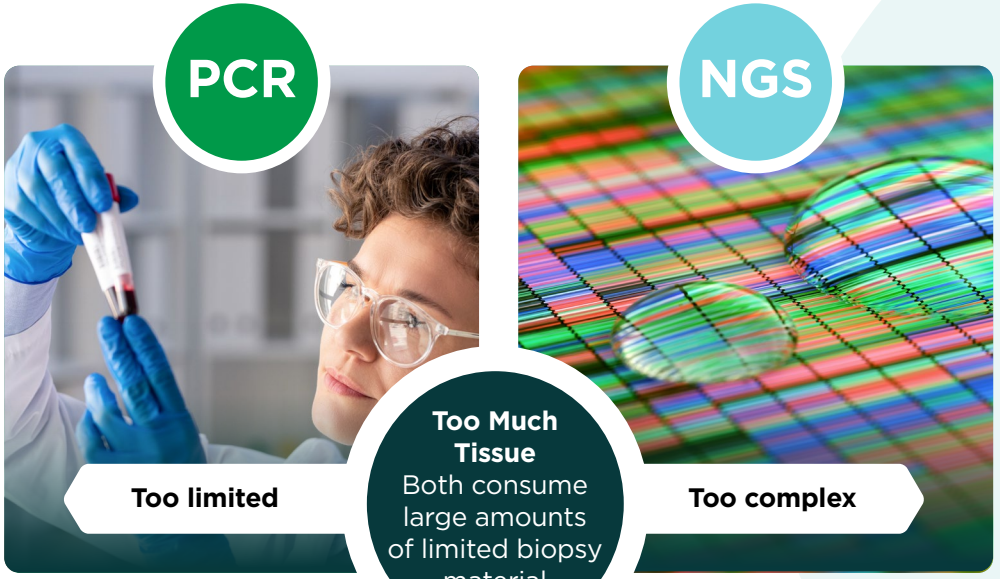
Genomic biomarkers in cancer are generally detected through one of two different methods – polymerase chain reaction (PCR), and next generation sequencing (NGS).

Due to the limitations of these technologies, oncologists are often faced with one of two challenges:

1. Not enough information to accurately identify the best potential treatment options.
2. Slow results, with too much complex information that confuses the decision process.

Not Comprehensive
Limited to sequential single gene testing, which impacts the ability to find all actionable mutations.

Not Sensitive
Lacks sensitivity for detecting actionable mutations (~ 2-5% VAF).



Too Slow
4-5 weeks for test results.

Too Complex
Requires >100 steps, cannot test for DNA mutations and RNA fusions simultaneously. Highly skilled lab personnel a must.

Too Costly
As much as $5,000 per test.

ASPYRE – A Dramatic Technological Breakthrough

ASPYRE is a completely new molecular technology that enables more patients to experience the benefits of targeted therapies by overcoming the limitations of PCR and NGS technologies.

Fast - patients can go from diagnosis to actionable biomarker results in 2 days. Total lab processing time is less than a day.

Actionable – one assay to identify all NCCN guideline-approved biomarkers associated with FDA-approved targeted therapies.

Sensitive - Up to 10x more sensitive than NGS, and 50x more sensitive than PCR.

Low sample requirements – significantly reduces tissue needed.

Simple – straightforward 4-step workflow on existing infrastructure. No need for bioinformatics.

Low Cost – suitable for repeat testing.

ASPYRE – The Science Behind the Breakthrough

At the heart of the ASPYRE technology is an enzymatic reaction called pyrophosphorolysis, or reverse DNA polymerization.

This unique chemical reaction activates a synthetic probe only when a target mutated molecule is present in a patient sample, enabling the probe to then be amplified and detected.

The extreme specificity of the reverse polymerization reaction enables ASPYRE's ultra-sensitive single-molecule detection.

By amplifying synthetic probes instead of sample DNA, ASPYRE has the same optimal conditions for all markers, allowing a single test to simultaneously analyze hundreds of biomarkers across multiple genes without sacrificing performance or speed.

ASPYRE requires just 4 reaction steps, which can be completed by non-specialist laboratory staff in a matter of hours.

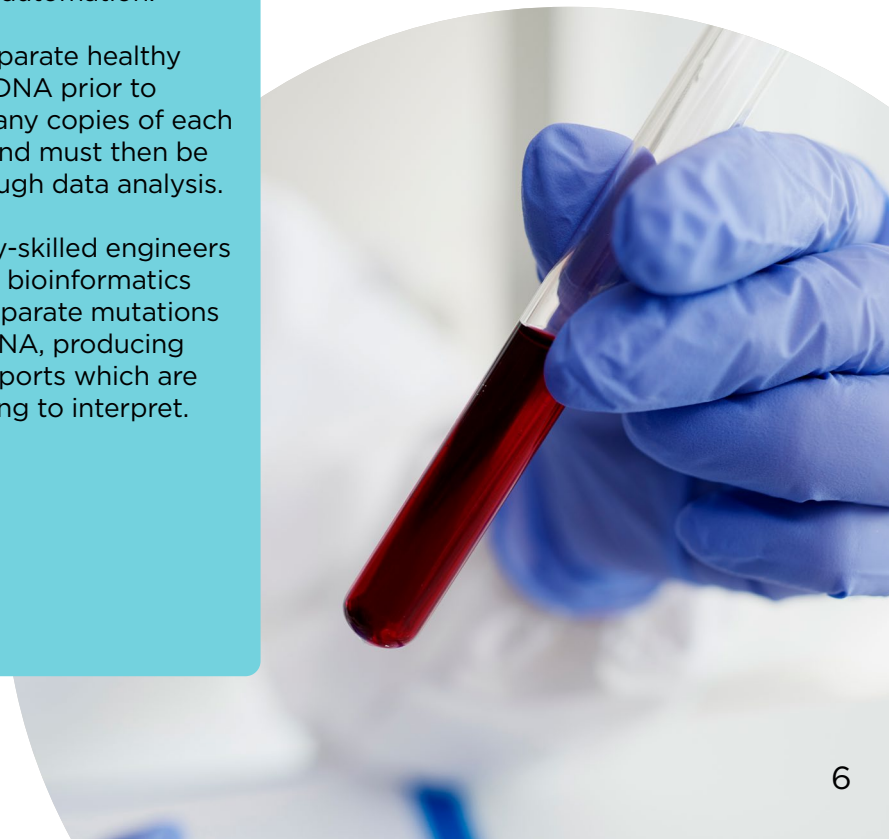
Probes can be replicated millions of times, enabling detection on existing PCR instruments, with simple data analysis.

NGS – Complex Workflow & Data Analysis

Traditional NGS technologies involve hundreds of steps, requiring skilled staff, complex workflows and automation.

NGS cannot separate healthy from mutated DNA prior to sequencing; many copies of each are analyzed, and must then be separated through data analysis.

Teams of highly-skilled engineers utilize complex bioinformatics programs to separate mutations from healthy DNA, producing complicated reports which are often challenging to interpret.



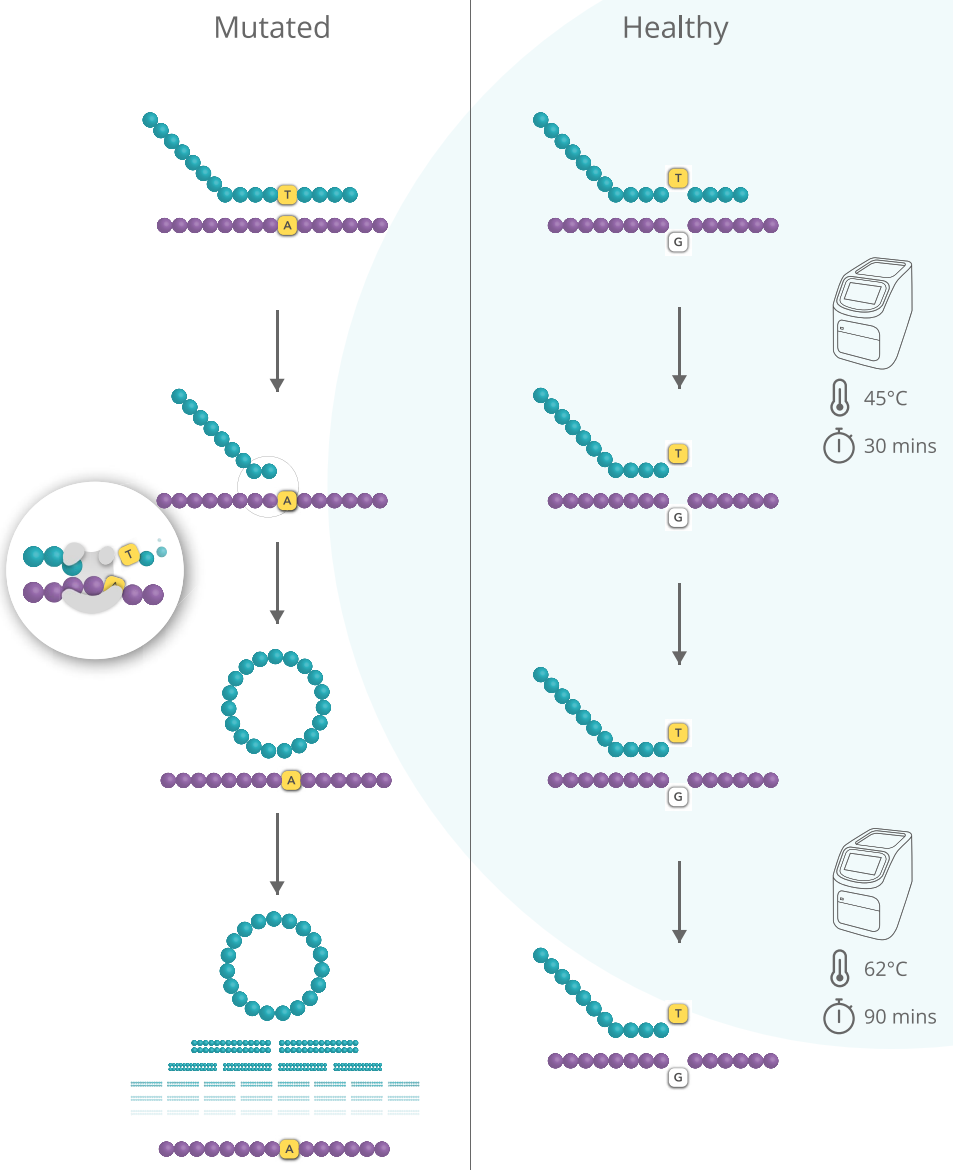
The ASPYRE Reaction

1. ASPYRE probes hybridize to both healthy and mutated DNA but are mismatched to healthy molecules.

2. Reverse polymerization specifically digests only perfectly-matched probes. Those annealed to healthy DNA are not digested due to mismatch.

3. Digested probes are selectively circularized by ligation.

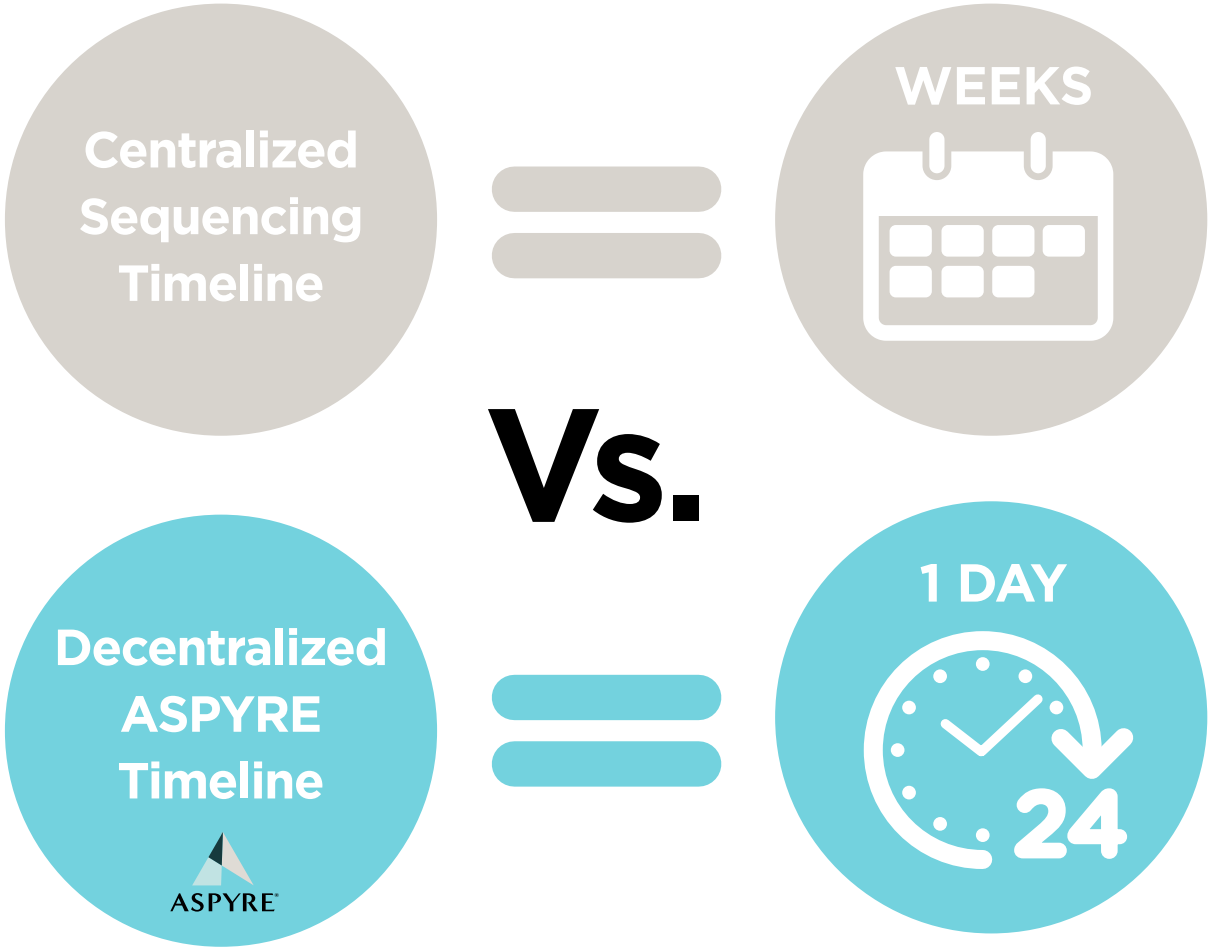
4. Only circularized probes are amplified and detected. Probes that hybridized to healthy molecules are not amplified.



Democratization of Biomarker Testing

Next Generation Sequencing in Centralized Labs takes weeks to generate test results.

ASPYRE can be run in less than a day using standard PCR instruments.



Decisions vs. Discovery

In contrast to NGS, ASPYRE is focused on delivering only the clinically evidenced, actionable information needed for optimal treatment decision making.

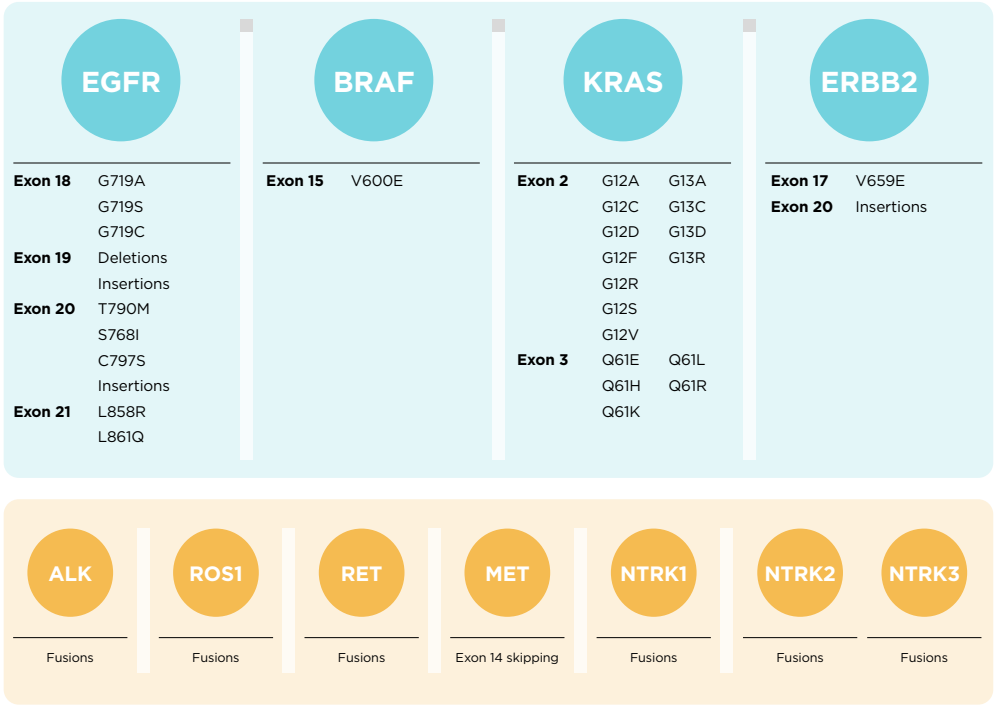
The National Comprehensive Cancer Network (NCCN) guidelines identify biomarkers across 11 genes that are associated with FDA-cleared targeted treatments for non-small cell lung cancer (NSCLC).

The ASPYRE-Lung panel simultaneously tests for 77 DNA mutations and 37 RNA fusions across these genes, delivering actionable results within hours.

By simplifying the detection of these key mutations from either tissue or blood, use of ASPYRE-Lung as a first-line diagnostic identifies those patients who will benefit from targeted therapy at a fraction of the time and cost of NGS.

Simple reports, easy to interpret.

Clinically evidenced, actionable information.

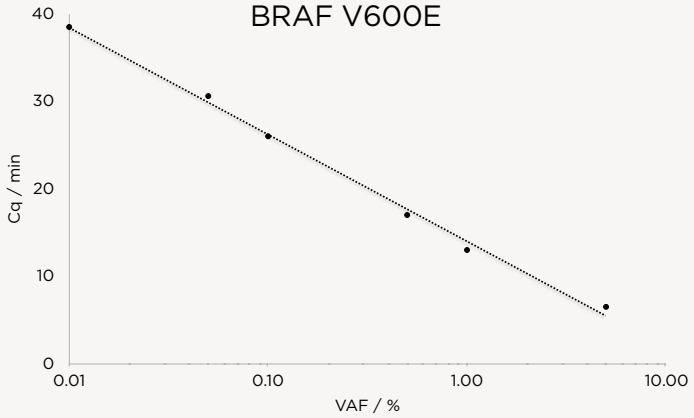


Detects Mutations at an Earlier Stage

ASPYRE uses unique synthetic probes to detect actionable biomarkers without interference from background DNA, providing extremely high sensitivity and specificity.

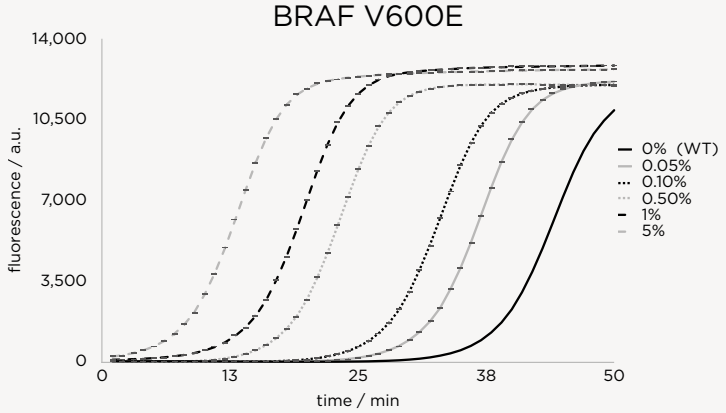
ASPYRE's unique molecular reaction allows the detection of actionable biomarkers from tissue or blood at 0.1% Variant Allele-Fraction (VAF) or less, even if just a single mutated molecule is present in the sample.

Best-in-Class Sensitivity



- Published data demonstrated 100% sensitivity at 0.1% VAF or below.*
- Ability to detect as little as a single molecule of mutated DNA or RNA.
- Overcomes sensitivity limitations inherent in poor efficiency of NGS sample prep.
- High sensitivity maintained from as little as 1ng input DNA.

Extremely High Specificity & Repeatability



- Very high specificity; crucial to ensure correct treatment decisions and for accurately detecting rare mutations.
- Consistent performance and results across FFPE* tissue and plasma samples.
- High degree of repeatability with very low sample-to-sample variation.

*Silva et al (2021) Nature Scientific Reports 11:6068 https://doi.org/10.1038/s41598-021-85545-3

*FFPE = Formalin Fixed Paraffin Embedded

Low Sample Requirements

ASPYRE significantly reduces the amount of material needed to generate fast, comprehensive biomarker results from either tissue or blood. This ensures that treatment options are not limited due to the quantity of the tissue sample or delayed by the need for more biopsies to obtain additional tissue.

It is estimated that as many as 20-35% of lung tumor biopsy samples are inadequate to fulfill molecular profiling needs.

Lower sample requirement has the potential to reduce test failure rates, and overcomes challenges of insufficient DNA quantity or quality.

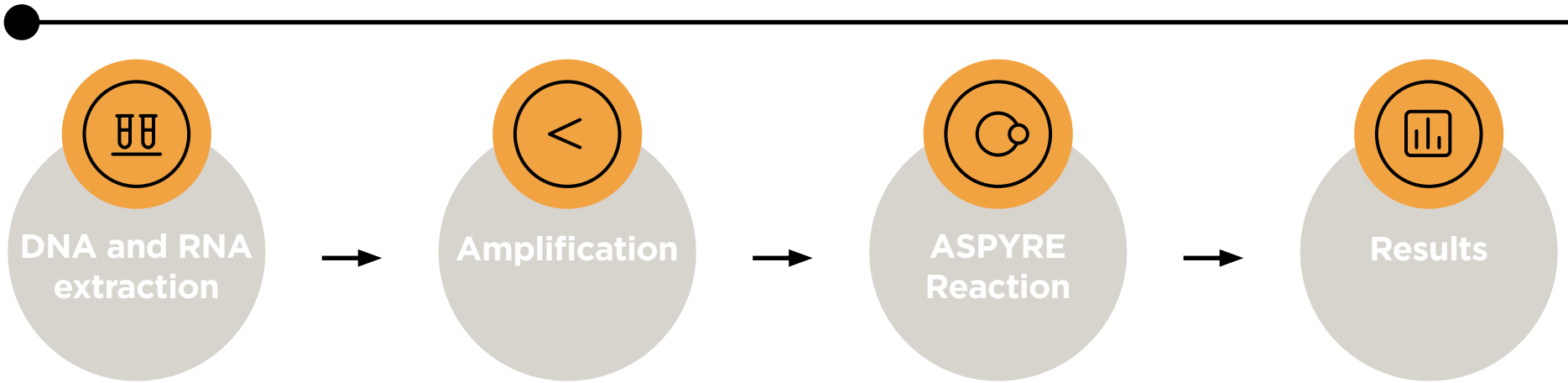
Single-molecule sensitivity
ASPYRE's unique chemical reaction amplifies mutations from single molecules, meaning actionable mutations can be detected from a low number of tumor cells without the need to perform invasive and risky re-biopsies. The unique probes can be replicated millions of times, ensuring accurate biomarker detection even with a minimal amount of tissue.

Blood or tissue analysis
A single kit can be used to test from either blood or tissue.

Benefits of Liquid Biopsy

- Less invasive.
- Reflects heterogeneity within the tumor tissue, including clonal somatic variants.
- Allows fast molecular testing without exhausting precious tissue sample.
- Readily enables testing during treatment to monitor changes in the patient's molecular profile.

Straightforward Workflow and Automation



Standard sample preparation

- DNA and RNA can be extracted using single kit/protocol and run through assay simultaneously on a single instrument.
- Workflow requires only the addition of reagents & incubation – no intermediate purification steps nor clean-ups are required.
- Hands-on tech time < 30 minutes.
- The multiplexing capabilities of ASPYRE avoid the need to divide sample between multiple assays, reducing sample requirements.
- Large or small numbers of samples can be run with similar costs per sample; no requirement to batch multiple samples per run.

Reduces the Cost of Biomarker Testing

ASPYRE is a highly cost-effective diagnostic tool for identifying actionable mutations, using batch sizes ranging from one to many samples.

As a result, it has the potential to increase the number of patients who undergo biomarker testing, which means more patients will have the opportunity to benefit from highly effective targeted therapies.

The low cost of ASPYRE also makes it suitable for routine monitoring of patients to detect treatment resistance at the earliest possible stage. This will prevent patients from continuing to receive therapies that no longer provide clinical benefits.

- Standard sample processing.
- Simple, straightforward workflow using low-cost reagents.
- Ability to analyze multiple genes and biomarkers in a single assay.
- No new equipment or outsourcing needed.
- No bioinformatics or complex data analysis.

ASPYRE

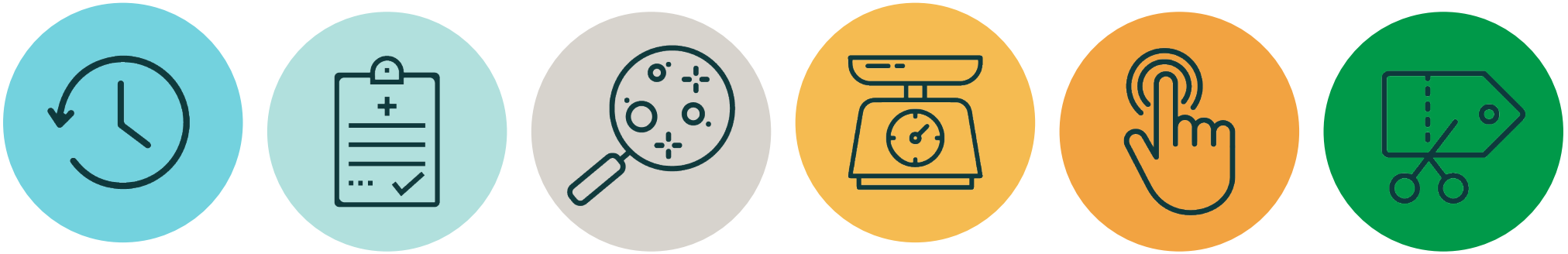
Fast, comprehensive, actionable biomarker detection

	PCR	ASPYRE	Sequencing
Workflow	1-2 steps	4 steps	>100 steps
Multiplexing	Single gene (10's mutations)	Multi-gene (100's mutations)	1000's genes
DNA/RNA	Separate runs	Simultaneous on one instrument	Separate runs
Turnaround time	< 1 day	1 day	7-14 days
Sensitivity	~2-5% VAF	0.1% VAF	~0.2-2% VAF
Ease of adoption	Simple Existing PCR equipment	Simple Existing PCR equipment	Complex Centralized testing and expensive instrumentation
Scalability	No sample batching	No sample batching	Batching of samples
Cost	$	$	$$$$

ASPYRE®

ASPYRE - A Truly Breakthrough Technology

Breaks Down the Barriers to Optimized Therapy for All



Fast | **Actionable Results** | **Ultra Sensitive** | **Minimal Sample** | **Simple Workflow** | **Cost Effective**

Biofidelity.

Bringing high-precision diagnostics to millions of underserved patients.