

PERSONALIZED MEDICINE

An Update on Our Long-Term Investment Thesis

Introduction

At Aristotle Atlantic Partners, LLC (Aristotle Atlantic), a pillar of our investment process is identifying secular themes. These are long-term trends characterized by significant, multi-year shifts in spending patterns driven by consumers, governments, or corporations. In September 2020, we published a white paper introducing personalized medicine as one of these themes. In the six years since, several regulatory, clinical, and commercial milestones have provided meaningful support to our thesis and broadened the associated investment opportunity set. This Thought Piece is intended to update investors on how our thinking has evolved.

Personalized medicine is an approach to healthcare that customizes diagnostic testing and therapeutic intervention to the unique biological characteristics of an individual patient. Traditionally, diseases have been diagnosed based on symptoms and treated with generalized regimens. Personalized medicine instead seeks to identify the specific molecular, genetic, or physiological features of a given patient's disease and to tailor treatment accordingly. The aim is to deliver better patient outcomes, reduce adverse side effects, and lower overall system costs by minimizing the use of ineffective and expensive therapies.

The Enabling Technology Backdrop

The rapid progress of personalized medicine since 2020 reflects the coming together of two enabling technology trends that, in our view, deserve particular attention. The first is the dramatic, sustained decline in the cost of genetic sequencing. What cost billions of dollars to accomplish in the early 2000s can

Key Takeaways



Personalized medicine has moved from an emerging technology story into a commercial and clinical reality, with multiple FDA approvals, guideline inclusions, and Medicare coverage decisions since 2020.



Liquid biopsy, initially used to guide therapy selection in advanced cancer patients, has extended into recurrence monitoring, therapy response monitoring, and, perhaps most importantly, primary screening of asymptomatic patients.



The addressable opportunity has broadened beyond oncology into women's health, organ health, and multi-cancer detection, supported by an expanded set of investable companies.



Two related sub-themes have emerged: monetization of the proprietary clinical data these diagnostic platforms generate, and continuous physiological monitoring through medical-grade consumer wearables.



We continue to believe personalized medicine offers attractive long-term investment opportunities and that we remain in the early stages of a multi-decade shift.

today be done for a few hundred dollars per genome, making comprehensive genomic profiling economically viable at population scale. This cost decline has extended the reach of personalized medicine beyond advanced-stage cancer patients, where the per-test cost is easiest to justify given the clinical benefit, into much broader populations for screening, recurrence monitoring, and general disease surveillance.

The second is the rapid advancement of artificial intelligence and machine learning. Interpreting genomic and molecular data is a complex, high-dimensional problem, and recent advances in AI have made it possible to identify meaningful clinical signals in datasets that would previously have been analytically intractable. The combination of low-cost sequencing generating vast amounts of biological data, and machine learning tools increasingly capable of finding structure and meaning within it, is, in our view, the underlying engine that has moved personalized medicine from an aspirational concept into a viable commercial reality.

From Emerging Technology to Clinical Reality

When we first identified personalized medicine as an investable secular theme in 2020, our thesis was anchored by an early conviction in liquid biopsy, the practice of using a blood sample rather than a tissue sample to identify tumor-specific mutations and guide cancer care.

Whether performed on blood or on tissue, the underlying diagnostic workflow is commonly referred to as comprehensive genomic profiling (CGP): a single test that simultaneously assesses hundreds of cancer-relevant genes to identify actionable mutations, gene fusions, and other alterations that can be matched to targeted therapies. Where a traditional single-gene or small-panel test answers one narrow question, CGP produces a broad molecular portrait of a patient's tumor in a single workflow, which is a substantially more efficient use of both patient samples and clinical time.

In 2020, CGP was principally used for therapy selection in advanced-stage cancer patients: a valuable but relatively narrow clinical application. Since then, the underlying technology has moved decisively into two much larger use cases: post-treatment monitoring for cancer recurrence and, perhaps most importantly, primary screening of asymptomatic patients for the presence of cancer.

One of the most significant developments, in our view, was the U.S. Food and Drug Administration's July 2024 approval of Guardant Health's Shield blood test for colorectal cancer screening in adults 45 and older, followed almost immediately by a favorable Medicare coverage decision. This non-invasive option arrives at a critical time, as more than one-third of eligible adults, or roughly 50 million people, currently skip recommended screenings according to the American Cancer Society. Since the FDA approval, Shield has been added to the National Comprehensive Cancer Network's colorectal cancer screening guidelines and has received coverage under the Veterans Affairs and TRICARE health programs. In our view, this sequence of events represents the clearest validation to date of liquid biopsy's move from a niche oncology tool into a platform technology with population-scale screening applications. Primary cancer screening is by far the largest addressable use case for the technology, and one we highlighted as the long-term prize in our original paper.

Personalized medicine's recent progress has not been confined to diagnostics. In August 2026, Moderna and Merck announced that their investigational personalized mRNA cancer vaccine, intismeran autogene, combined with Keytruda, met its primary endpoint in a Phase 3 trial of adjuvant therapy for high-risk resected melanoma. The vaccine is custom-manufactured for each patient by sequencing their tumor and encoding up to 34 of its unique mutations into a bespoke mRNA therapy. This first late-stage success for an individualized neoantigen vaccine is an important proof point that personalized medicine's reach extends well beyond diagnostics into therapy design itself.

Expanding Applications

Alongside primary screening, minimal residual disease (MRD) monitoring has emerged as a second major growth vector for liquid biopsy. MRD testing uses a blood test after cancer treatment to detect residual disease molecules at levels far below what conventional imaging can identify, informing decisions about additional therapy or extended surveillance. Multiple providers are building commercial franchises in this application, and in our view MRD is following the same commercial trajectory that therapy-selection liquid biopsy did several years earlier: growing clinical evidence, inclusion in treatment guidelines, and expanding reimbursement coverage.

Personalized medicine is also reshaping how biopharmaceutical companies develop drugs. Using CGP and liquid biopsy to identify patients with specific molecular profiles allows drug developers to enrich clinical trials with those most likely to respond to a

given therapy, which can improve both trial success rates and the economics of oncology research and development. MRD testing is now playing a related role: in April 2024, an FDA advisory committee voted unanimously in favor of accepting MRD negativity as a surrogate endpoint for accelerated approval in multiple myeloma, a decision that could substantially shorten future oncology trials. This can result in faster time to market, longer effective patent life, and lower trial costs for biopharmaceutical companies, and a deeper structural role for diagnostics providers in bringing new therapies to market.

The success of liquid biopsy in oncology has also validated its use in adjacent applications. The same underlying cell-free DNA technology can be adapted for non-invasive prenatal screening, where fetal genetic conditions can be identified from a maternal blood sample; for carrier screening, where prospective parents can be tested for recessive genetic conditions they may pass on to a child; and for organ transplant monitoring, where the presence of donor-derived DNA in a recipient's bloodstream can be used to detect early signs of transplant rejection long before clinical symptoms appear. Each of these represents a large, growing end market in its own right. As a result, the investable universe has grown from the pure-play oncology diagnostics companies of 2020 to include a broader set of diagnostics providers operating across multiple large end markets in healthcare.

New Sub-Themes: AI-Enabled Data and Continuous Monitoring

As personalized medicine has evolved, we believe two related opportunities have emerged that merit specific attention.

The first is the monetization of proprietary clinical and molecular data. As a diagnostics company runs more tests, it accumulates a valuable proprietary dataset that, when linked to clinical outcomes over time, can be licensed to pharmaceutical and biotechnology customers for drug discovery, clinical trial matching, and biomarker research. Companies that can pair large, proprietary testing volumes with an AI-enabled data platform are, in our view, best positioned to capture value on both sides of the personalized medicine chain: the diagnostic test itself, and the data it generates thereafter.

The second is the extension of personalized medicine beyond the clinical setting into medical-grade consumer wearables and continuous physiological monitoring. In 2024, the FDA cleared the first over-the-counter continuous glucose monitor, expanding the addressable population from insulin-dependent patients to

the much larger population interested in metabolic health more generally. Consumer devices such as the Apple Watch continue to expand their ability to flag health conditions like atrial fibrillation using built-in sensors. In our view, the combination of continuous physiological data, on-device machine learning, and clinical integration is progressively extending personalized medicine from an episodic clinical event into a continuous, real-time care model.

Investment Opportunities

The market for personalized medicine diagnostics and monitoring is broad, spans multiple end markets, and is difficult to size precisely given how rapidly the space is evolving. In our view, the sustained revenue growth generated by leading providers is the clearest evidence that adoption is accelerating. Several companies held across Aristotle Atlantic strategies appear, in our view, particularly well positioned to benefit from the personalized medicine theme:

-  **Adaptive Biotechnologies.** Commercial-stage biotechnology company focused on the adaptive immune system, with a leading FDA-cleared blood test for minimal residual disease in blood cancers.
-  **Guardant Health.** Leading provider of liquid biopsy solid tumor cancer diagnostics across the care continuum, including therapy selection, recurrence monitoring, and primary cancer screening.
-  **Tempus AI.** Technology company pairing next-generation sequencing diagnostics with a proprietary multimodal clinical and molecular data platform licensed to pharmaceutical and biotechnology customers.
-  **Dexcom.** A leading provider in continuous glucose monitoring for the management of diabetes, with an expanding footprint in consumer metabolic health through its over-the-counter Stelo biosensor.
-  **Revolution Medicines.** Clinical-stage oncology company developing a pipeline of oral RAS inhibitors for RAS-mutated cancers, one of the most common classes of cancer-driving mutations, across multiple solid tumor types.
-  **Immunome.** Clinical-stage targeted oncology company developing antibody-drug conjugates and other targeted cancer therapies, with lead asset varegacestat in Phase 3 trials for desmoid tumors.
-  **Olema Pharmaceuticals.** Clinical-stage biopharmaceutical company developing targeted therapies for women's cancers, with lead candidate palazestrant in Phase 3 trials for ER-positive, HER2-negative metastatic breast cancer.
-  **Thermo Fisher Scientific.** Global leader in life sciences tools and services, supplying the instruments, consumables, and sequencing systems that enable personalized medicine across diagnostics and biologic therapeutics.
-  **Repligen.** Specialty bioprocessing company providing the chromatography, filtration, and process analytics tools used in the manufacture of biologic drugs, including targeted therapies central to personalized medicine.

Conclusion

We first wrote about personalized medicine as an investable secular theme in 2020, when the enabling technology was promising but largely unproven at scale. Six years later, in our view, the thesis has been meaningfully validated: liquid biopsy has secured FDA approval and Medicare coverage in its highest-value use case, MRD has emerged as a second commercial

franchise, AI-enabled data monetization has become a real business model, and continuous wearables are extending the theme into everyday consumer health. We continue to believe we are in the relatively early innings of a long-duration shift and remain excited about the investment opportunities the theme presents.

The companies listed herein represent all holdings across Aristotle Atlantic strategies classified within the Personalized Health secular theme as of September 30, 2026.

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