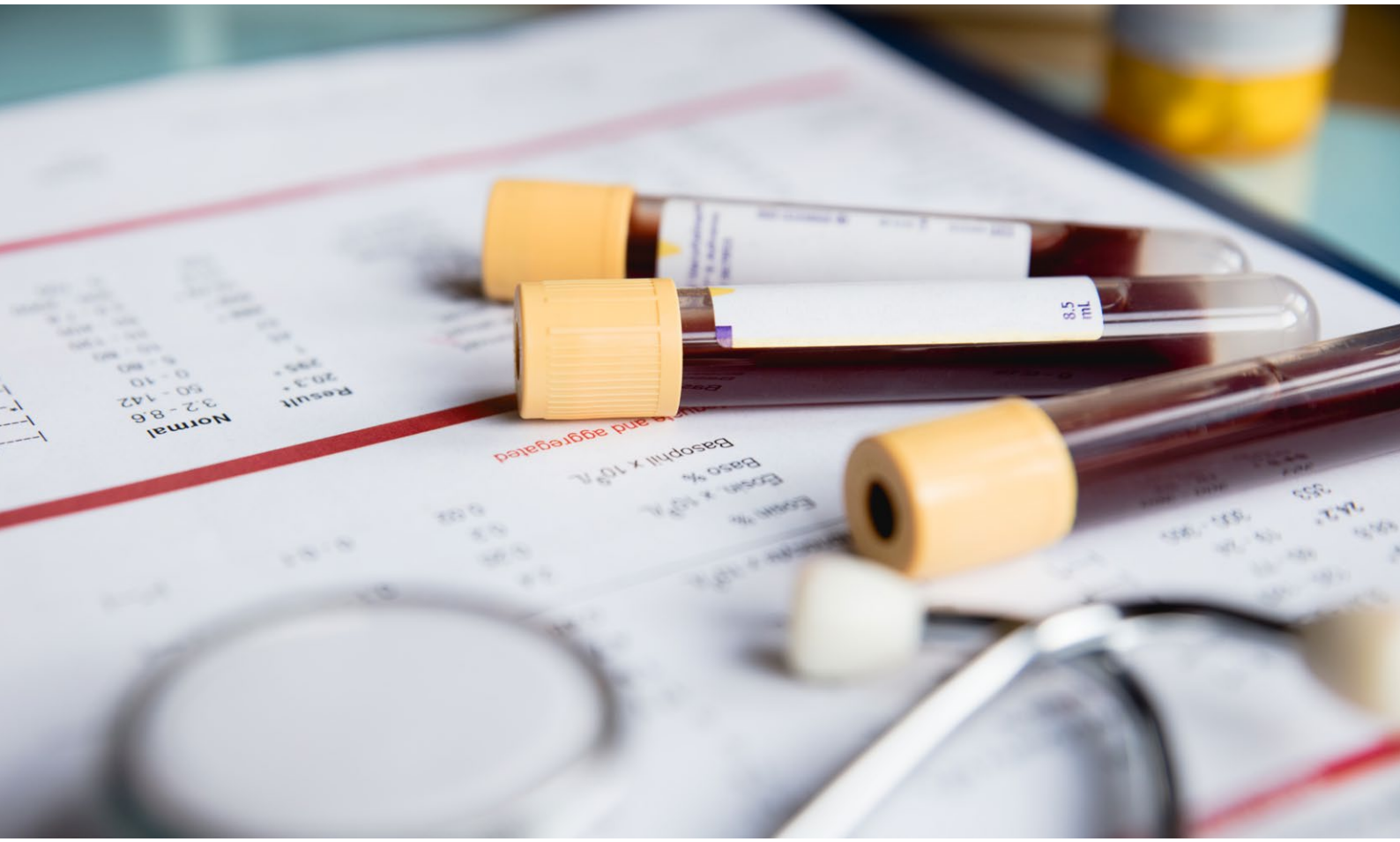


5 Strategies to Make Innovative Diagnostic Biomarkers a Success

Diagnostic biomarkers are vital in determining whether a patient has a particular medical condition as well as finding an effective treatment. Therefore, exploring and developing new biomarkers is prerequisite for impactful medical practice, however, this proves often to be a risky endeavor. What are alternative strategies for successful diagnostic biomarkers' development and commercialization?

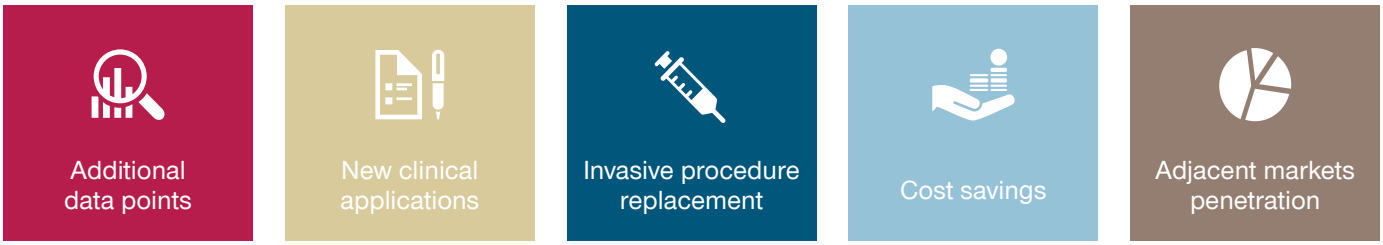
Biomarkers: By **definition**, diagnostic biomarkers are objective and quantifiable characteristics of biological processes. Also dubbed as molecular whistleblowers, they are able to show pathological changes, but also biologically normal body processes. Biomarkers known to everybody are, for example, a high body temperature that indicates fever or a high blood sugar level that signals diabetes.

Diagnostic biomarkers' capabilities make them very useful when it comes to the early diagnosis of certain diseases, the evaluation of the need and effectiveness of treatments as well as the assessment of the progression of certain diseases. Therefore, successful medical care relies on having the perfect biomarker for every illness. However, exploring and developing new biomarkers is a time-consuming and expensive endeavor, with high uncertainty in terms of return on investment.

5 strategies to make innovative biomarkers a success

Whether it is to prioritize biomarker R&D efforts or to maximize the uptake of a biomarker which has already been developed, there are a number of strategies which should be considered to be ultimately successful. Due to our in-depth knowledge of the field and vast industry experience, we were able to pick the top five strategies:

5 strategies to make biomarkers a success



1. Generate data points to provide clinical decision support

Uncertainties around treatment decisions are common and unnerve patients as well as healthcare providers. A sound fact base with clear data points can be used to reduce these doubts, which is key and highly needed especially in the case of major implications for patients' health and quality of life. Biomarkers for BRCA1 (breast cancer gene 1) and diagnostic tools like Axumin and NephroCheck, which are using biomarkers, provide these data base and therefore reduce the treatment burden for healthcare professionals (HCPs) and patients by guiding treatment decisions and preventing over-treatment.

A famous best practice example is **Angelina Jolie**, who underwent a bilateral risk-reducing mastectomy (BRRM) after a pathogenic BRCA1 mutation indicating up to 87 percent risk for hereditary breast cancer had been detected through **Myriad's BRACAnalysis test**. Before BRCA testing, BRRMs were uncommon as HCPs based their risk assessment largely on family history. With BRCAnalysis, the risk can be assessed more accurately and test results may prevent or delay the onset of cancer or detect it at an earlier, more treatable stage. Together with more frequent coverage by insurers and Angelina Jolie's role model function, this has led to a steep **increase in prescriptions of BRCA testing** since 2011.

Another example: Approximately **20 to 40 percent of patients experience recurring prostate cancer**. Whereas location and determination with current methods is challenging, Bracco Imaging's positron emission tomography (PET) tracer Axumin enables an earlier change in clinical management leading to more accurate treatment decisions. Within the first two years after its launch in 2017, close to 10,000 unit sales in the US have been reported with over 50,000 patients being diagnosed by Axumin.

Another highly relevant case where biomarker data acts a superior decision support: risk assessment for acute kidney injury (AKI). Delayed diagnosis of AKI can increase the length of hospital stays, personal and financial costs as well as follow-up costs for additional treatment due to irreversible injury. Astute Medical's NephroCheck is a novel AKI biomarker test designed to meet the need for risk assessment in AKI regarding patient AKI severity and when to initiate dialysis. A key driver for the adoption of NephroCheck is the perceived enhanced treatment certainty through novel AKI biomarker testing, because it provides superior value over existing diagnostic options to improve patient outcomes and reduce healthcare expenses.

This showcases that biomarkers providing clear treatment implications in a disease area with a high treatment uncertainty are the optimal playground for biomarker uptake maximization.

2. Monitor and foster new clinical applications for your biomarker

Not all biomarkers will realize their full potential in the first years after launch. As the treatment landscape evolves, new clinical applications might arise. This development is in particular driven by new treatments that require a **companion** or complementary diagnostic.

One example for this dynamic is FeNO (fractional exhaled nitric oxide) testing in asthma treatment. A FeNO test measures the level of airway inflammation in an asthma patient's expired breath. After the discovery of FeNO's role in biological processes in the 1990's, FeNO's clinical application was focused on initial asthma diagnosis as well as on the likelihood of responsiveness and adherence to inhaled corticosteroid treatment. Back then, international asthma guidelines did not recommend FeNO as a routine test for asthma patients due to the lack of conclusive evidence. Reimbursement inclusion failed multiple times for the same reason in many markets.

Around 2019, this started to change with the availability of new biologic treatments (omalizumab, dupilumab) in the asthma space. FeNO measurement now acts as complementary diagnostic and has a new clinical application: helping to identify candidates for biologic therapy. This development transformed market dynamics and potentials for FeNO testing: First, **international asthma guidelines recommended FeNO** for the new clinical application. Second, additional countries decided to reimburse FeNO testing. For example, **FeNO testing is reimbursed in Germany** since 2020 for determining eligibility for treatment with dupilumab.

This example shows that it's important to actively monitor new treatments on the horizon. Doing so will allow you to realize your biomarker's full potential. In addition, continued data creation beyond single clinical applications helps you to explore new opportunities and engage at the right time.

3. Replace invasive diagnostic procedures with non-invasive biomarkers

Another strategy to increase the use of a biomarker is to get both specialists and patients to request its use. For this to happen, you must develop a biomarker that is less invasive and therefore safer and more comfortable for the patient than current methods. The therapeutic areas in which an invasive procedure such as a biopsy could be replaced by a biomarker are countless, for example by diagnosing celiac disease without colonoscopies:

In the case of celiac disease, current diagnostic tests with a celiac-specific antibody for this disease deliver satisfactory results, but still require a fairly invasive endoscopy. To replace the endoscopy, several promising biomarkers are under investigation for screening and diagnosing patients with celiac disease. Considering that an estimated **one percent of the population has the disease**, and that a **high percentage of these patients are not diagnosed**, a successful candidate could achieve a high uptake relatively quickly.

Another application area for this strategy could be colorectal carcinoma. It's the third most common cancer in the United States and its early detection is vital to increase patients' chances of survival. However, currently the only reliable **method of screening is invasive and inconvenient**, the colonoscopy. This leads to many patients being diagnosed late and facing serious consequences. Many manufacturers such as Exact Sciences with Cologuard or Roche have therefore been seeking a solution to this problem. The development of a biomarker that could avoid a colonoscopy or at least make it only necessary when there is a high risk of illness will most certainly be successful.

Whereas **Roche has not been able to complete the development**, the high demand of **over 2 million people screened since launch** fueled the strong growth of Exact Sciences's Cologuard leading to a revenue over 199 million US dollars in 2019.

4. Consider health economics and invest in tests that save money

Current reimbursement processes often do not adequately take into account the value of your tests with regards to complexity and clinical value. Achieving or maintaining high prices for your tests and broad usage of your biomarkers are not mutually exclusive. Investing in data that shows the cost-effectiveness of your assay due to reduced costs of therapy and quality-adjusted life year (QALY) will provide you with a strong fact base to receive the full value of your biomarker.

For example, tumor profiling tests such as EndoPredict, Oncotype DX Breast Recurrence Score, and Prosigna provide significant clinical value by reducing burdensome chemotherapy in women with HR+ or HER2- breast carcinoma in the early stage. However, these tests were widely considered to be expensive assays by payers in many countries. For example, the cost for Oncotype DX Breast Recurrence Score is around 3,400 dollars in the US, based on Medicare reimbursement rates. However, multiple international studies showing cost-effectiveness due to chemotherapy avoidance and QALY of test use provided a huge evidence base. The growing economic evidence base has led to reimbursement in several countries, e.g. US, Canada, UK and Germany.

5. Strengthen your brand equity through a portfolio of innovative biomarkers

Roche, the market leader in cardiac biomarkers, offers diagnostic tests for a variety of cardiac conditions like heart failure (NT-proBNP), acute coronary syndrome (Troponin), and atrial fibrillation (GDF-15). As such, Roche is the perfect example of an IVD company developing its portfolio of biomarkers in adjacent therapeutic areas.

In the 1990s, BNP was used as a cardiac marker, however, it was not completely reliable. Back then, researchers at the University of Oslo also discovered a biomarker, NT-proBNP, which promised much better results. Roche negotiated with them to obtain a license to develop and market the NT-proBNP biomarker. The company did not just put it on the market, but invested heavily in developing clinical trials to prove the value of the NT-proBNP, so that although its initial success was only because of its value in the diagnosis of acute heart failure, it is now recognized as the **gold standard in heart failure management and considered and recommended by numerous clinical guidelines**.

By entering adjacent markets, not only is there no need for you to make a (brand) name for yourself, but you are able to make better use of your sales force by leveraging your existing network and client base and by adding a new complementary product to your specialized sales rep's bag.

Conclusion: Several roads lead to success in biomarker development

As you can see, there is more than one strategy to successfully explore and develop new biomarkers. To reduce development time and expenses and maximize a return on investment, you should make sure that your innovative biomarker meets at least one of the following criteria: It provides data points as a better decision basis, has the potential to expand into new applications, is a less-invasive procedure than current standard of care diagnostic tools, saves money, or completes your company's portfolio. If this applies, you are in an excellent position to effectively maximize the market uptake of your biomarker.

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