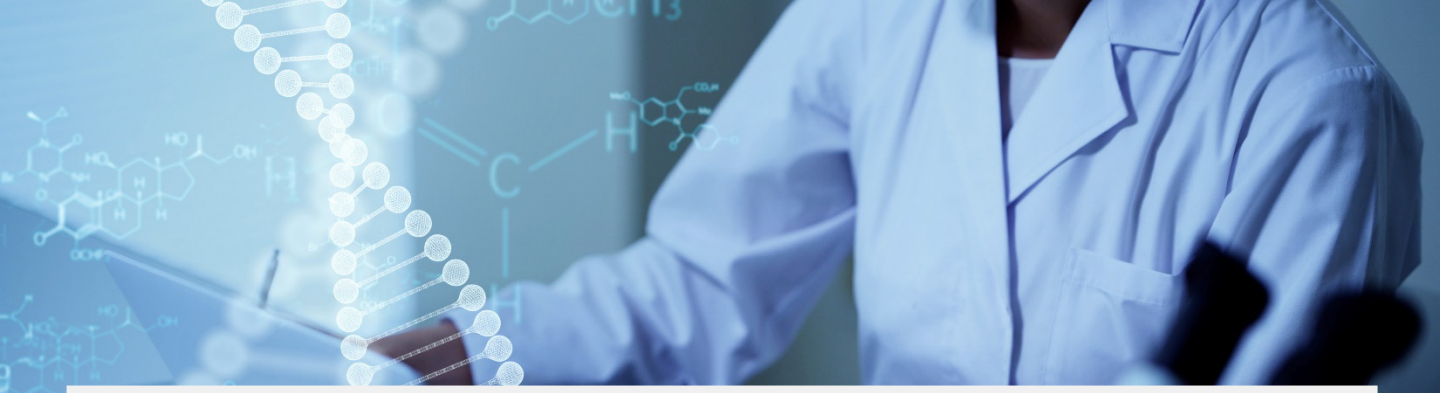
ThermoFisher SCIENTIFIC

Genetic insights for biopharmaceuticals: Propelling drug candidates into therapeutic assets

applied biosystems



Rising R&D investment in clinical trials

How are research and development resources allocated within the biotechnology and pharmaceutical industries?

In this white paper, you will learn:

- How genetic analysis is enabling more rapid and efficient clinical trials
- How integration of genetic analysis technologies is evolving in the pharma and biotech spaces
- How Thermo Fisher Scientific genetic analysis solutions may enable you to gain competitive advantage

For biopharmaceutical and biotechnology companies, innovation is imperative. Economic growth in these industries relies heavily upon investment in product development—perhaps more so than any other industry during this period of global demand for infectious disease prevention, surveillance, and treatment as well as tremendous advancement in discoveries towards precision medicine. In 2019 alone, the US pharmaceutical industry invested $83 billion on research and development (R&D), roughly 10-fold compared to the entire decade from 1980–1989 (adjusted for inflation). Not only is absolute investment growing at a tremendous rate, R&D spending as a share of net revenues is rising as well, from averaging 19% from 2005–2014 to over 25% in 2018 and 2019.[1] The nebulous risk in bringing biopharmaceutical assets to market makes a truly rigorous estimation of new drug development costs extremely challenging. However, best estimates range from a few hundred million dollars to over two billion dollars, accounting for as many of the panoply of expenditures and risks as possible. For biopharmaceutical developers, optimizing R&D investment in new technologies is essential to gain and sustain a competitive edge.

Clinical trials present a tremendous opportunity to leverage advanced genetics technologies and practices to improve efficiency and reduce cost. While the variability among clinical trials is vast and complex, a 2020 publication explored the causative factors of cost efficiency of clinical trials involving novel therapeutic agents.[2] According to this study, the two most significant factors influencing trial cost are the number of patients required to instantiate a treatment effect, and the number of clinic visits taken by those patients throughout the trial. Genetics technologies can identify disease and drug response biomarkers and pathogen genes to reveal genetic factors that may either put a person at risk or suggest a positive outcome, helping to screen trial participants early and optimize cohorts to maximize trial efficiency. Genetic information can also reveal risk factors which can be used to ensure participant safety. Quantitative analyses can also be performed to assess efficacy and dosages of biotherapeutics. With more stringent cohort screening, clinical investigators may be able to accelerate the pace of their clinical trials, thereby propelling their drug candidates through the pipeline, all the while minimizing expenses.

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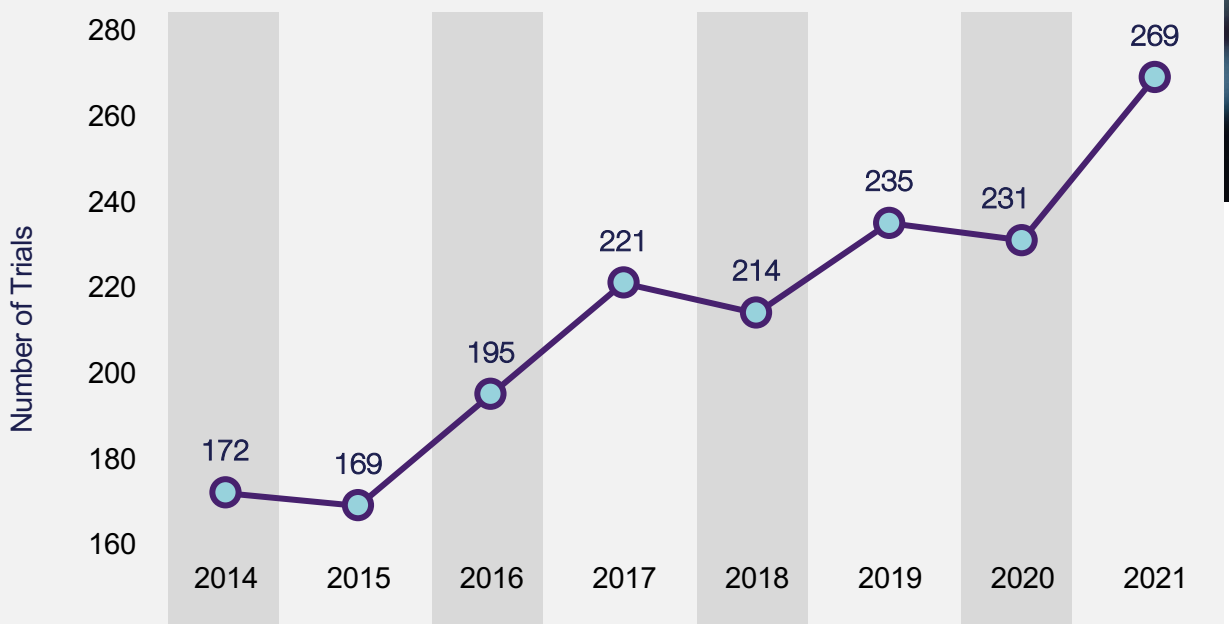
1 U.S. Congressional Budget Office (2021) Research and development in the pharmaceutical industry. https://www.cbo.gov/publication/57126.

2 Moore TJ et al. (2020) Variation in the estimated costs of pivotal clinical benefit trials supporting the US approval of new therapeutic agents, 2015-2017: a cross- sectional study. *BMJ Open* 10(6):e038863.

The next evolution in clinical trials

Strategic investment in genetic analysis technologies optimizes and expedites clinical trials

56% increase over 7 years in clinical trials involving qPCR, dPCR, CE, or MA



Trials involving the four genetic analysis techniques by start date from 2014-2021.

Source: GlobalData

As R&D spending continues to climb, drug developers are turning to technology providers who deliver comprehensive and flexible genetic analysis tools that enable robust, innovative, and strategic asset development. Technologies that yield new insights into the human genome are beginning to fulfill expectations for the value of biopharmaceuticals in precision medicine.

Thermo Fisher Scientific genetic analysis technologies enable new approaches for biopharmaceutical R&D. Integration of genetic analyses into preclinical and clinical studies aids in the assessment of the efficacy and safety of biopharmaceuticals. Quantitative genotyping, gene expression, and variant analysis can reveal biomarkers, expression, localization, and interactions of biopharmaceutical agents such as monoclonal antibodies, mRNA- and protein-based vaccines, and cell- and gene-based therapeutics. Thermo Fisher Scientific genetic analysis technologies have also become fundamental to pharmacogenomics and disease risk-stratification research.

New strategies for biopharmaceutical asset development are driving R&D investment, particularly in genetic analysis technologies that can help to optimize and expedite clinical trials. From 2014 through 2021, over 1,700 clinical trials involving qPCR, dPCR, capillary electrophoresis (CE) or microarray (MA) genetic analysis technologies were initiated. This number is growing, from 172 trials commenced in 2014 to 269 by the end of 2021, a 56% rise over the period.

What explains the rise in enthusiasm for these genetic analysis techniques?

Genetic analysis is used by all sponsor types

Industry organizations sponsor 40% of all clinical trials involving genetic analysis

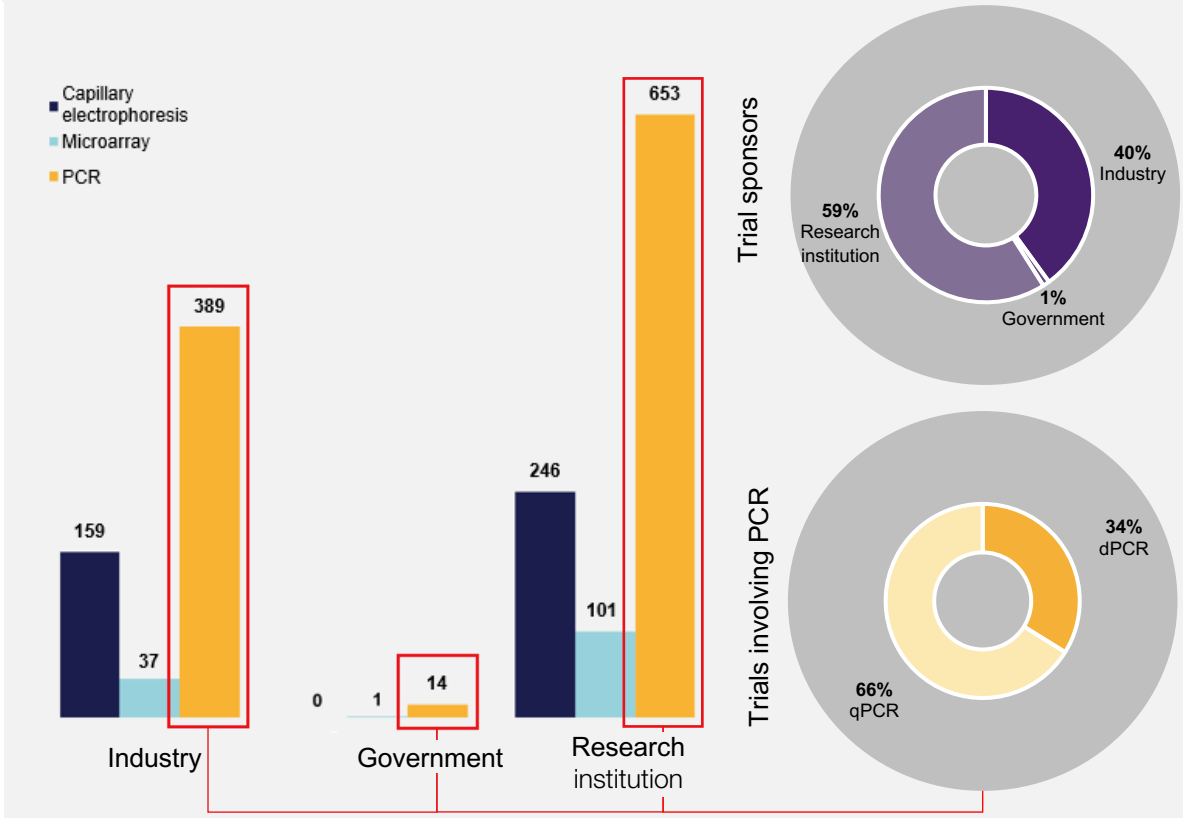
Competition in the biotechnology and pharmaceutical industries is heating up, leading companies to search for tools to accelerate clinical trials and improve time to market.

With the hope of accelerating developmental products to commercialization, many companies are turning toward genetic solutions to guide this initiative. All genetics technologies covered in this analysis provide utility across the landscape of clinical applications and organizations. Of clinical trials that are using genetic analysis technologies, 59% of sponsors are academic and research institutions, and 40% are industry organizations. Government sponsorship is negligible. Among all trials, regardless of sponsor type, qPCR and dPCR are the most used genetic analysis technologies at 65%.

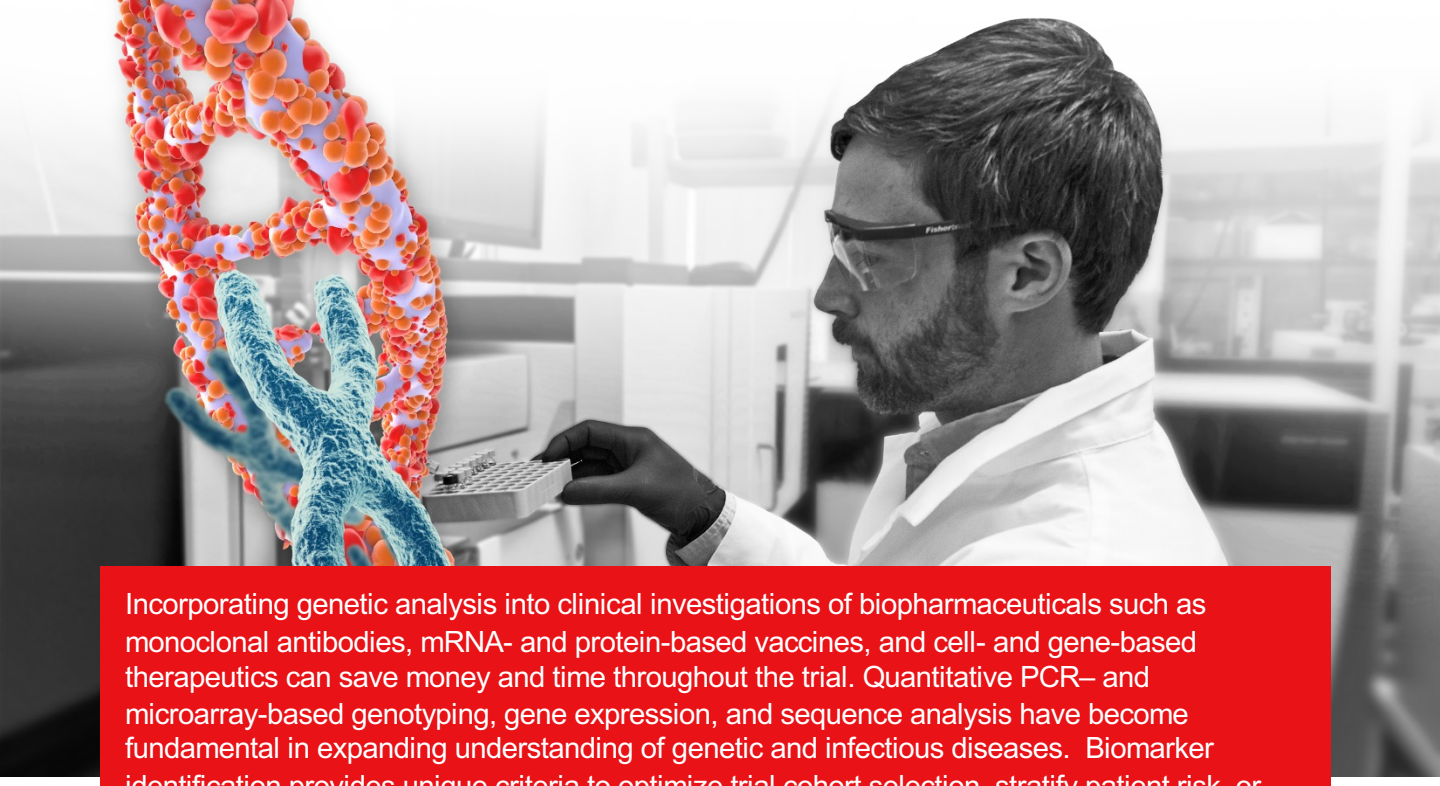
Research institutions have been leading genetic analysis deployment in clinical trials, but industry organizations are close behind.

Since 2014, 291 industry organizations have sponsored trials involving genetic analysis throughout the drug development process.

Industry sponsors conducted 40% of the clinical trials involving genetic analysis, with quantitative PCR as the dominant technology



Distribution of genetic techniques among trial sponsor types (left) and qPCR:dPCR split across all sponsors types (right) from 2014-2021.
Source: GlobalData



Incorporating genetic analysis into clinical investigations of biopharmaceuticals such as monoclonal antibodies, mRNA- and protein-based vaccines, and cell- and gene-based therapeutics can save money and time throughout the trial. Quantitative PCR– and microarray-based genotyping, gene expression, and sequence analysis have become fundamental in expanding understanding of genetic and infectious diseases. Biomarker identification provides unique criteria to optimize trial cohort selection, stratify patient risk, or tailor treatment. Oncology trials are an especially informative example. Drug developers are using genetic analysis to explore every therapeutic modality to prevent and treat cancer. In cancer trials, clinical attrition rates are particularly high. Risk stratification and pharmacogenomics can have tremendous benefits for both clinicians and patients. This opportunity is reflected in the prevalence of oncological indications in the pool of all trials leveraging genetic analysis.

Genetic analysis is used in trials for many diseases

Oncology dominates clinical investigations among all sponsors that use genetic analysis technologies

49% Oncology therapy area

23% Infectious disease therapy area

20% Other therapy areas

4% Hematologic disorders

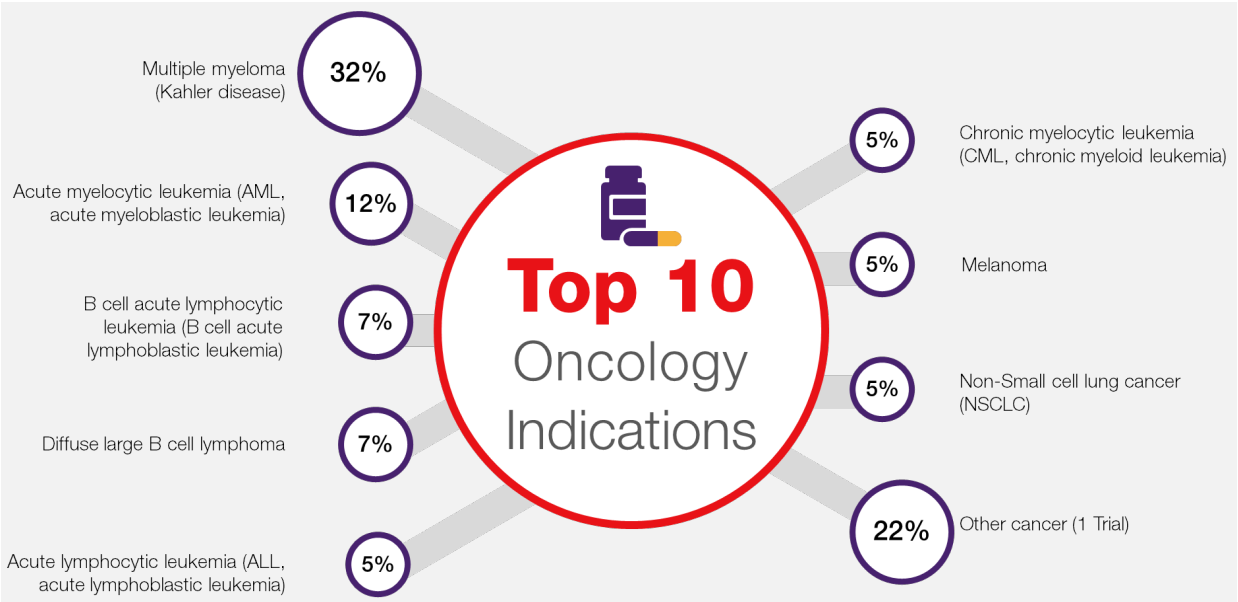
4% Metabolic disorders

Source: GlobalData

Genetic analysis is used in trials for many diseases (cont.)

Multiple myeloma dominates in industry-sponsored oncology trials that involve genetic analysis technologies

When comparing different cancer types in industry-sponsored oncology trials, multiple myeloma stands out from other cancer indications with 32% of trials across all drug development phases, followed by acute myelocytic leukemia (12%), B cell acute lymphocytic leukemia (7%), and diffuse large B cell lymphoma (DLBCL) (7%). Genetic analysis allows for the quick identification of the type of hematopoietic cancer.

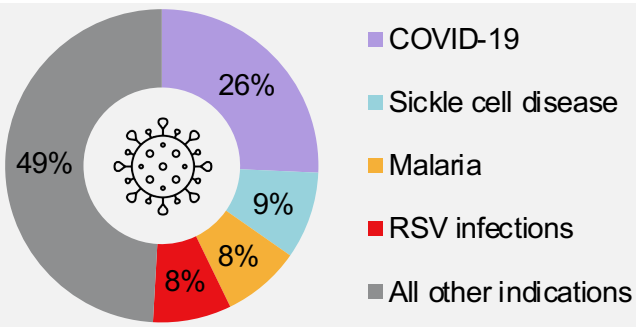


Most common industry-sponsored oncology trial indications involving genetic analysis technology from 2014-2021.
Source: GlobalData

COVID-19 trials represent more than a quarter of industry-sponsored non-oncology trials that use genetic analysis technologies

Among industry-sponsored trials other than oncology trials, COVID-19 accounts for the greatest number of trials. The demand for COVID-19 vaccines and treatments, and expectations for biopharmaceutical solutions, has led to a surge in infectious disease trials. Genetic analysis is used to localize points of infection, quantify viral load, evaluate response to vaccine or treatment, and investigate the reason for great differences in individual response. Genetic association studies are helping determine drug priorities by identifying variants associated with COVID-19 illness, thereby increasing chances of eliciting a treatment response and maximizing trial success. Other predominant non-oncology indications are sickle cell disease and malaria, and genetic analyses may similarly help increase the chances of success against these illnesses.

Non-oncology industry trials are highly clustered among four indications from 2014-2021



Source: GlobalData

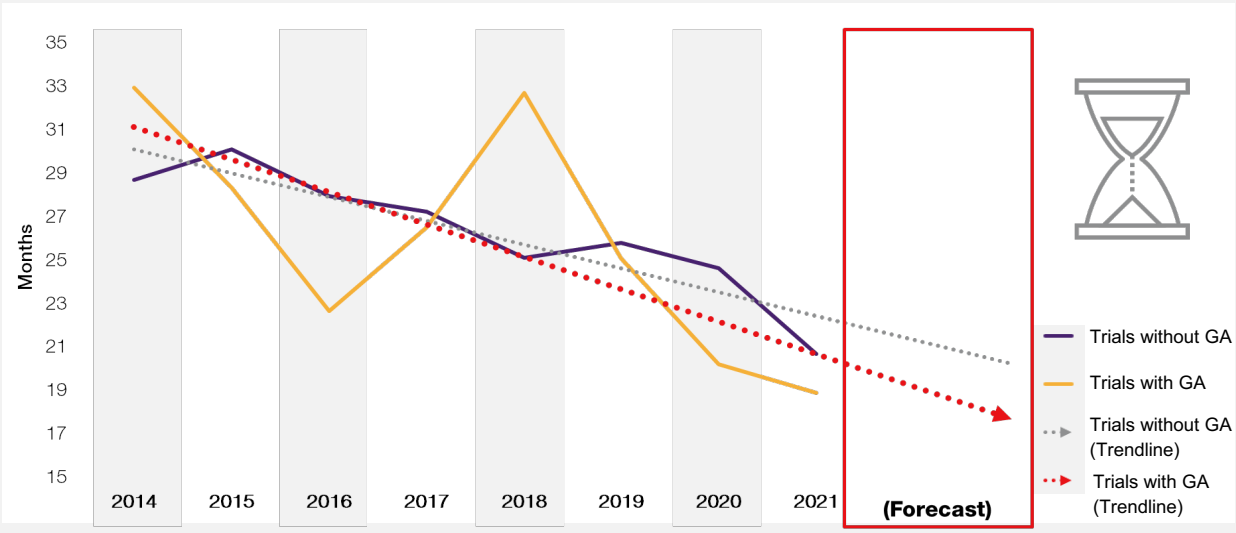
Trials using genetic analysis have shorter enrollment periods

Genetic analysis enables fast screening of potential trial participants

Genetic analysis can yield valuable insights across the gamut of therapy areas and throughout the clinical trial framework. To appreciate the value genetic analysis can bring to clinical trials, we compared a single parameter (time to complete trial enrollment) in phase I/II oncology trials with and without incorporating genetic analysis.

Among trials that use genetic analyses, cancer trials account for more than twice the number of trials for the second most prominent indication (infectious disease). (Note that clinical investigation of infectious diseases is currently driven disproportionately by the recent COVID-19 pandemic.) Regarding the drug development pipeline, 55% of all currently active trials are in phase II. **The opportunity to use genetic analysis to shorten enrollment periods is substantial and forecasted to continue growing.**

Cohort enrollment periods are shorter in phase I/II oncology trials that use genetic analysis technologies



The impact of qPCR, dPCR, microarrays, and capillary electrophoresis on enrollment period of phase II (including combined phase I/II) trials from 2014–2021, including forecast trendline. **Note:** GA = Genetic analysis Source: GlobalData

dPCR, qPCR, microarrays, and capillary electrophoresis can be used to quickly screen potential cohort participants for relevant biomarkers or pathogen infection. Clinical trials using genetic analysis technologies have had shorter enrollment periods than otherwise comparable trials

- **Shorter every year** since 2014*
- **0.74 months quicker** in 2019
- **4.42 months quicker** in 2020
- **1.84 months quicker** in 2021
- Forecasted to be **3.53 months quicker** in 2025

* Except 2018

Global business trends

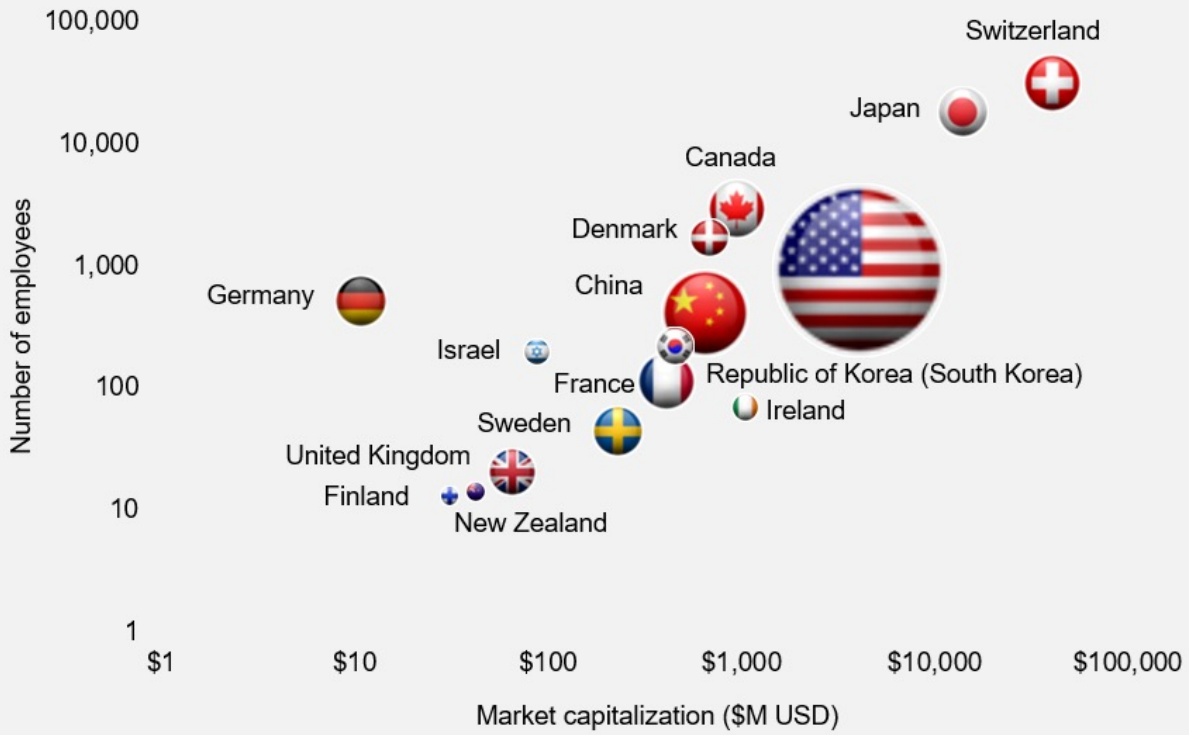
How companies around the world deploy genetic analysis

Companies around the world and of all sizes are leveraging genetic analysis tools to expedite their clinical trials. On the one hand are juggernauts, like Novartis, Johnson & Johnson, Celgene, and Amgen, that have begun more than twenty such trials since 2014. On the other hand, there are many companies with a single genetic solution–enabled trial over the same time period. For this reason, it is worth exploring the long tail of this distribution and identifying trends among these sponsors.

Among the international pool of industry sponsors with just one trial incorporating genetic analysis, the United States emerges as the most prolific with 81 single-trial companies currently, primarily in oncology and infectious disease. The US is trailed by China, with 20 single-trial companies, also in oncology and infectious disease. Canada, France, and Switzerland all contain nine companies having conducted single trials with genetic technologies over the eight-year period.

The remaining analyzed countries also make excellent candidates for genetic analysis implementation, as its ability to maximize efficiency in clinical resource allocation can provide scaling opportunities to grow even the leanest development portfolio. For example, the average Ireland-based company with one genetic analysis trial has around 70 employees and a market capitalization of over one billion USD. While their clinical development is presumably operating efficiently, ramping up deployment of genetic technologies would enable scaling of their pipeline while maintaining their current strength of high marginal employee productivity. Conversely, companies with many employees but relatively low market capitalization, such as Germany, have clear need for efficiency maximizing solutions. Regardless of location within the clinical development matrix, genetic analysis offers myriad opportunities to amplify productivity and efficiency in clinical development.

Companies around the world that include genetic analysis in their trials

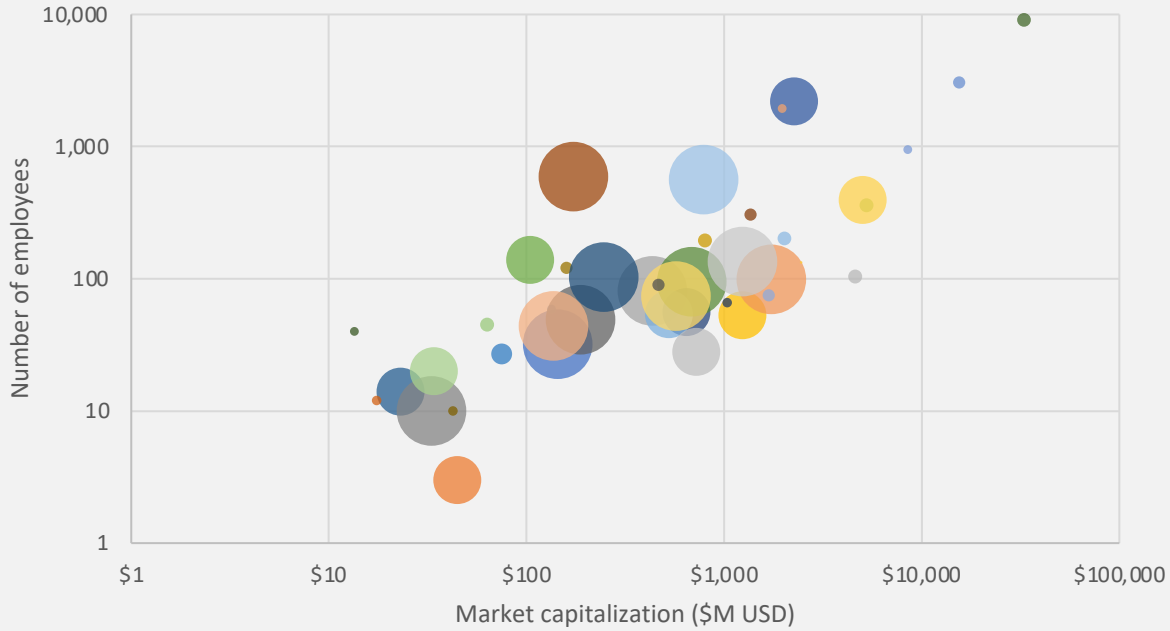


Average market capitalization and employee count of public companies with one trial including genetic analysis from 2014-2021.
Note: Bubble size represents the number of companies with a trial that involves the use of genetic technology. Accurate economic analysis in some countries is made challenging due to varying levels of corporate privatization and transparency.
Source: GlobalData

The US companies that are running one clinical trial using genetic technologies are in private and public sectors. Over 50% of these trials are conducted by public companies. These companies cluster strongly on the orders of 1 billion USD market capitalization and 100 employees, suggesting that many small companies are developing pharmaceuticals that are garnering tremendous interest from investors. Although genetic analysis can improve the developmental capabilities of any company, the therapy area in which it is being employed can provide a great deal of information regarding individual use cases.

Each bubble represents a company's single trial, while the size of the bubble reflects the prevalence of the therapy among the pool of all genetic analysis trials initiated since 2014. In other words, oncology–the most common therapy area overall is represented by the largest bubble, followed by infectious disease, and so on, down to the smallest bubble representing underdeveloped therapy areas, such as genito-urinary system and sex hormone disorders. As one might expect, companies clustering strongly at the means are utilizing genetic analysis for oncology trials, a risk-averse development strategy. Interestingly, the companies with the highest market capitalizations are leveraging genetic analysis in some therapy areas that are historically unusual, such as immunology and genetic disorders. Not only is genetic analysis continuing to support legacy trials like those in oncology and infectious disease, it is also being used experimentally to equip companies with the tools necessary to innovate and expand into new therapeutic frontiers.

US companies using genetic analysis in a variety of therapeutic use cases



Average market capitalization and employee count of US public companies with one genetic solution trial from 2014-2021.
Note: Bubble size represents genetic trial indication prevalence among pool of all trials involving genetic analysis. Different bubble color represents a different company's trial.

Source: GlobalData

Whether your priority is to expedite your clinical trial process with advanced genetic analysis technologies or to pivot existing genetic techniques to other areas of high value, the utility of these technologies to add efficiency to your biopharmaceutical asset development can bring essential competitive advantage to your programs.

Incorporating genetic analysis into clinical investigations can provide early insights into mechanisms of action, efficacy and safety of candidate biopharmaceuticals.

Microarrays
- Genotyping
- Pharmacogenomics
- Copy number analysis
- Risk stratification
- Reproductive health

Capillary electrophoresis
- Targeted variant analysis
- Molecular profiling

dPCR
- Rare-allele detection
- Absolute target quantitation

qPCR
- Variant identification
- Targeted gene expression of diverse sample types

Thermo Fisher Scientific offers genetic analysis solutions that span the drug development process. Contact us to learn more about how our solutions can help expedite your therapeutic to the market

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