INORGANIC GROWTH STRATEGIES IN PRECISION MEDICINE

Forging New Paths to Value Creation in the Future of Healthcare

CROSSTREE

Table of Contents

Introduction

During the last decade, the pharmaceutical industry has rapidly evolved from a model focused on development of blockbuster drugs for large patient populations into a market delivering targeted therapeutics to narrow segments of the population, aiming to improve patient centricity and improve the quality and cost burden of health care. This "precision medicine" approach may be new to most consumers, but the concept has been steadily shaping the healthcare and life sciences industries for over a decade.

Precision medicine improves the performance of health systems by aiming to improve patient centricity and developing a better understanding of disease causes and treatment consequences, thereby providing measures to improve the quality and cost of health care being provided to patients.[1]

Specifically, precision medicine helps reduce costs associated with trial-and-error dosing, hospitalizations due to adverse drug reactions, late-stage health condition diagnoses, and reactive treatments. It can also play a crucial role in the implementation of value-based payment and delivery models, thus helping in the better coordination of patient care and cost reduction initiatives.[2]

While it is often thought that precision medicines are so specialized as to prohibit significant sales, that isn't always the case. Analysts expect a Novartis gene-therapy treatment for spinal muscular atrophy, which hasn't yet reached the market, to generate $1.7 billion in sales by 2023 and to become one of the first precision medicine blockbuster drugs.[3]

Thanks to a confluence of cultural, technological, regulatory, and economic factors, advancements in Precision Medicine have skyrocketed in the past few years, resulting in rapid consolidation in the life sciences sector and unprecedented opportunities for value creation.

Precision Medicine: The Opportunity

Historically, the pharmaceuticals industry developed, manufactured, distributed, and marketed conventional drugs with largely homogeneous logistical and economic characteristics, resulting in mass-production efficiencies. Not surprisingly, the ecosystem of pharma services and diagnostics firms which serves this lucrative industry was also focused on supporting high volume pharmaceutical production. But beginning with practices as simple and commonplace as blood type matching, precision medicine has blossomed into one of the highest growth market segments of the healthcare industry, valued at ~$60 billion today and projected to grow to ~$100 billion over the next five years[4] and close to $800 billion by 2028[5].

For detailed valuation and transaction analysis, read our monthly BlueBooks at CrosstreeCapital.com/Insights.

In response to this shift from conventional to precision medicine, the entire pharma services ecosystem has also pivoted to enable more specialized, complex treatments and patient journeys. Over the past five years, biopharmaceutical companies nearly doubled their R&D investment in precision medicines and expect to increase their investment by an additional 33% in the next five years[6]. This burgeoning market for specialty and targeted therapies has caused a profound disruption among industry players. Success in the precision medicine market requires highly specialized expertise and technology as well as agility and responsiveness beyond anything the life sciences sector has ever seen.

Amidst such rapid and chaotic change lie significant opportunities for strategic and financial investors to create and enhance value. Firms in the Diagnostics Services, In Vitro, Life Science Tools, In Vivo, and Development sub-sectors of life sciences have seen their market valuations increase by an average of 58% in the past 12 months compared to the prior period (Fig. 1).

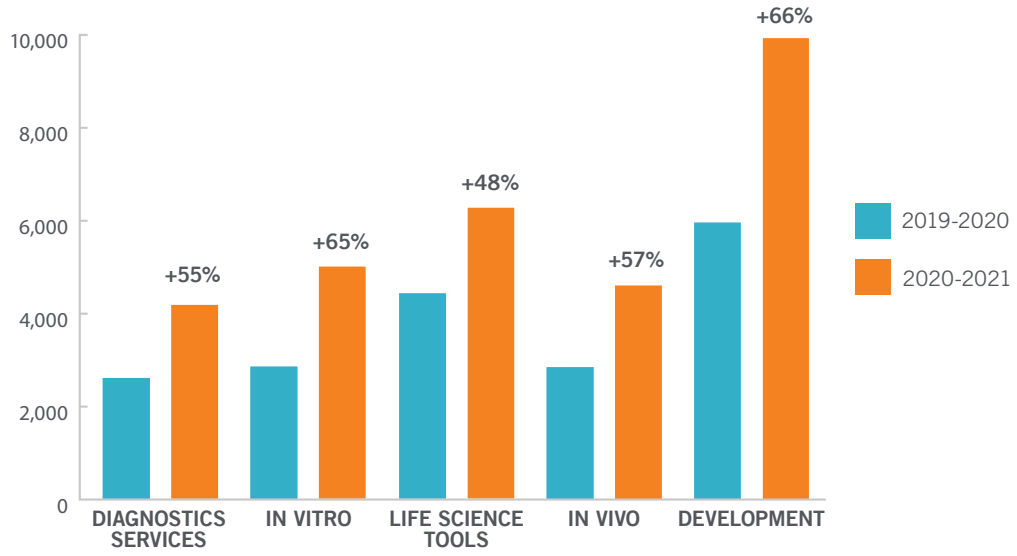

Figure 1: Market Valuation Averages for Life Sciences Firms

Growth Drivers of Precision Medicine

According to Global Market Insights, the United States and certain European countries are currently the major hubs for conducting and recruiting patient pools used in precision medicine trial applications in oncology, globally. A confluence of cultural, technological, regulatory, and economic factors is driving the rapid growth in demand for precision medicine. Among them:

COVID-19

Amid the COVID-19 pandemic, precision medicine is advancing with incredible speed. The Healthcare industry is focused on conducting precision medicine and genomics research to better understand COVID-19 susceptibility, measure its impact, and discover potential therapies. Precision medicine has spurred collaborative efforts between governments, medical institutions, and researchers to swiftly develop effective treatments. The entire healthcare industry has turned to precision medicine and genomics research to quickly understand human susceptibility to COVID-19, measure the virus' impact, and develop potential therapies.

RISING INCIDENCE OF CANCER

In 2020, close to 20 million people were living with cancer[7]. Gene characterization and sequencing is the leading method to gain information about genes and their probable mutations, boosting demand for personalized diagnostics and therapeutics for cancer, neurodegenerative diseases, and rare genetic conditions. In 2019, the National Institute of Health issued a grant of $3.7 million to the Washington University School of Medicine to fund an open-source database with the goal to boost Precision Medicine and genomic research for cancer, and in May 2020, the Minderoo Foundation and the Federal government granted $67 million for the Zero Childhood Cancer program (ZERO) to facilitate the development of a comprehensive genomic databank of individual patient cells for a better understanding of childhood cancer.

ADVANCEMENTS IN HUMAN GENOMICS, PHARMACOGENOMICS & MOLECULAR TECHNOLOGIES

In the last 15 years, the cost of mapping a human genome has dropped from $100 million to less than $1,000[8], allowing the use of data from patient DNA to become a viable method to provide precise, actionable recommendations. Advances such as next-generation sequencing (NGS) technologies have resulted in an unprecedented proliferation of genomic sequence data and with it, demand for access to large-scale human genome databases. Pharmacogenomics is the study of how genes affect an individual patient's response to therapies. This relatively new field combines pharmacology and genomics to help predict the efficacy of a drug in specific patient populations, speeding discovery timelines and improving the efficacy of biopharmaceuticals. Pharmacogenomics requires highly advanced tools and devices to enable the molecular analysis of humans and diseases, driving demand for more of these technologies.

REGULATORY APPROVALS & SUPPORT

According to studies conducted by the Personalized Medicine Coalition (PMC)[9,10], personalized medicines accounted for only 5% of new FDA approvals in 2005, but more than a third of approvals for three of the last four years.

The US Food & Drug Administration (FDA) continues to issue guidance and statements of support for precision medicine, despite the complexity the agency faces in dealing with these approvals.

About the PMC

In 2003, 20 institutions representing various sectors of the health system launched the Personalized Medicine Coalition (PMC) to advocate for changes that will increase investment in personalized medicine and facilitate its adoption.

> The vast amount of information generated through NGS poses novel regulatory issues for the FDA. While current regulatory approaches are appropriate for conventional diagnostics that detect a single disease or condition (such as blood glucose or cholesterol levels), these new sequencing techniques contain the equivalent of millions of tests in one.
>
> Because of this, the FDA has worked with stakeholders in industry, laboratories, academia, and patient and professional societies to develop a flexible regulatory approach to accommodate this rapidly evolving technology that leverages consensus standards, crowd-sourced data, and state-of-the-art open-source computing technology to support NGS test development. This approach will enable innovation in testing and research, and will speed access to accurate, reliable genetic tests[11].

Impact of Life Sciences M&A

The precision medicine market is highly competitive and consists of several large players and a long tail of small- to mid-sized firms. Although the pharmaceutical industry has historically been dominated by large companies able to extract value through economies of scale, success in precision medicine demands agility and innovation, offering market participants new paths to value creation regardless of size. To gain competitive advantage and capitalize on this rapidly evolving opportunity, life sciences firms and investors alike are seeking to quickly identify capabilities gaps and address them through highly targeted mergers and acquisitions.

The impact on M&A and financing deal volume and multiples has been nothing less than extraordinary. In the past 12 months (May 2020 – April 2021), the Diagnostics and Tools sub-sector saw 667 transactions - a 53% increase 12 months' volume. The Pharma Services sub-sector also saw an 11% increase in transaction volume, with 189 deals in the past 12 months (Fig. 2).

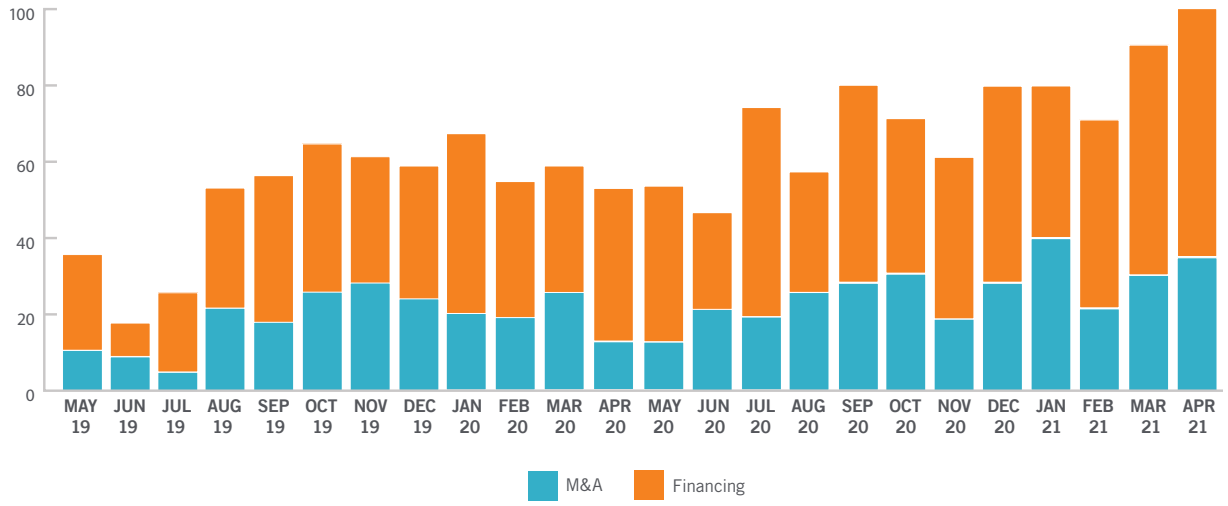

Figure 2: Monthly Deal Volume for Diagnostics & Tools and Pharma Services Firms

SUB-SECTOR IMPACT: PHARMA TECHNOLOGY & INFORMATION SYSTEMS

Over the past decade, novel technologies have allowed for the efficient and cost-effective development of precision and specialty medicines. The drug and device development space is poised to make further profound leaps in productivity, cost reduction and pace of innovation as it continues to embrace new technologies and methodologies and exploits them to their fullest potential. The value of this segment is rapidly increasing and expected to reach a market size of nearly $25 billion in the next five years[8].

Pharma Technology and Information Systems combines scientific aspects that are critical in the development and manufacture of new drugs, handling of medicines and medical devices with software, technology, eClinical solutions, and data subscription services to create an innovative value proposition though process standardization and increased efficiencies. Read more in Crosstree's Innovations in Pharmaceutical Development.

Innovative technologies ranging from cloud computing to distributed technology are being used to drive advancement in clinical trials, supply chain logistics and infrastructure efficiencies. Clinical research organizations, pharmaceutical companies, research laboratories, and investors in the drug development industry around the world have demonstrated the desire to accelerate drug and device trials and embrace new forms of validation in order to help speed the delivery of advanced cures and therapies to patients in need. Technical innovation in the clinical development space is driving growth, efficiency, and cost reduction in what is becoming one of the most promising drug and device development eras in recent history.

Precision medicine has driven such profound change in the capabilities needed by firms in this sub-sector, creating intense competition among strategic and financial investors to find and acquire firms with those capabilities in order to be first to market and capture the greatest value for their platforms.

DEAL INSIGHT

OVERVIEW

WCG acquired Los Angeles-based Trifecta Clinical to bolster its remote study startup and compliance support offerings.

SIGNIFICANCE

WCG is an industry leader delivering transformational solutions for clinical trials. They provide services that foster compliance and maximize efficiency for those in science and medicine, empowering their mission to develop the therapies and medicines that improve quality of life. By acquiring Trifecta, WCG adds remote study startup and compliance support to its suite of "Smart Trial" solutions.

LEARN MORE >>

SUB-SECTOR IMPACT: LABORATORY SERVICES

Laboratory Services are used to ensure the efficacy and accuracy of research data. The testing of research subject results of research therapies offers clinicians and researchers the necessary data to create safe and effective therapeutics with a minimum risk of errors. The increase in the number of sophisticated new medicines associated with precision and specialty medicines, such as human and tumor genetics, is helping to drive the uptake of large-scale laboratory services in the development market: approximately 80% of precision medicines require a diagnostic test or procedures.

The Laboratory Services market consists of companies that provide diagnostic testing ranging from blood tests to genetic analysis as well as other laboratory examinations of biospecimens derived from the human body for the purpose of providing clinical and research information for the effective development of novel treatments. Such services help deliver effective and efficient information needed in the development of new medicines and therapies. Read more in Crosstree's Innovations in Pharmaceutical Development.

Additionally, the need for adherence to international regulatory standards, is providing new opportunities for interoperability and automation of laboratory processes through innovative technologies. The implementation of automated solutions in laboratory workflows is enabling the processing of larger numbers of samples per unit of time, enhancing productivity and efficiencies while minimizing errors and costs. The integration of automated data management and the advent of increased accuracy and technologically advanced products, such as biochips and microarrays, as well as advanced diagnostic modes, such as companion diagnostics, is allowing for more cost-effective testing and development of novel therapeutics in the once extremely expensive realm of molecular, genetic and genomic testing.

SUB-SECTOR IMPACT: CLINICAL SERVICES

The global availability of a vast array of cost-effective services from drug discovery to post-marketing surveillance has allowed for the increase in near-virtual development of drug and device candidates for mid-size and small-scale organizations allowing them to direct otherwise scarce investment capital directly into expert-driven outsourced services rather than the creation of costly redundant and often less effective internal development efforts.

The Clinical Services market consists of companies who are supporting the development of new drugs and devices from inception through regulatory approval. Key drivers impacting the market's growth are globalization, new treatments in precision and specialty medicine, and the evolution in technology, all driving the rising demand for these more efficient and cost-effective third-party services and expertise. Read more in Crosstree's Innovations in Pharmaceutical Development.

The growing prevalence of precision and specialty medicine, such as gene therapies, to address disease and rare disease cases is expected to propel the clinical services market globally. The worldwide population has varied diseases and disease states not previously addressed due to a lack of effective technology to efficiently develop treatments for small population groups. The continued focus on individuals and small patient group treatments is expected to boost the clinical development of novel treatments for new and rare diseases.

DEAL INSIGHT

OVERVIEW

Advarra acquired Austin-based IntegReview and integrated its early-phase-focused, specialized IRB solutions into a center of excellence for the newly enhanced Advarra platform.

SIGNIFICANCE

Specialized solutions providers such as IntegReview — which exhibit agility, responsiveness, and a high-touch approach — complement technology-enabled IRB platforms, enhancing early phase capabilities. IntegReview excels at the accelerated timelines and nimble, white-glove requirements of early phase trials, which present significant challenges for most providers.

LEARN MORE >>

Developing Successful Inorganic Growth Strategies

Across almost all sectors - including life sciences - inorganic growth strategies can be broadly segmented into one of three categories:

- **Multiple Expansion**: increase size by acquiring more of the same general capabilities, creating value by capturing greater market share and revenue,
- **Capability Expansion**: enhance offering by adding complementary services or technologies, growing the value of the platform by leveraging higher value capabilities or assets, and
- **Geographic Expansion**: expand existing capabilities to new geographies, creating value by broadening customer base to include international and/or multi-national companies.

When applied to precision medicine, however, each of these strategies require a more nuanced approach than any other sector, because value creation in this space is dependent on the ability to identify and synthesize various highly specialized capabilities across the life sciences continuum, from molecular diagnostics to biobanks to CROs. These nuances impact the entire inorganic growth strategy development cycle, from platform analysis to transaction execution.

MARKET POSITIONING & CAPABILITIES GAP ANALYSIS

The precision medicine market continues to evolve rapidly, requiring granular insight into market players and trends in order to understand where a platform's capabilities stand. Resources such as off-the-shelf research reports are of little use in this dispersed market, in which the majority of companies are privately held (often founder-owned) with narrow, highly specialized capabilities and under $250m in revenue.

Leadership teams can provide deep insight into their own capabilities, but because their companies are so highly specialized, their insights come through the narrow lens of their particular slice of the market. Diagnostics company leadership will see market trends and competitors within the diagnostic space, but are understandably unfamiliar with, for example, the use of quantum computing in translational medicine and the development of virtual biorepositories, both of which intersect the diagnostics markets at critical junctures within precision medicine.

For these reasons, an expert, bottom-up analysis of all relevant players is necessary to accurately understand where a specific platform's capabilities fit into the big picture and identify gaps which must be filled in order to achieve long-term growth objectives. Only through this analysis comes a clear view of the current precision medicine market and a platform's position within it.

LONG-TERM STRATEGY DEVELOPMENT

Value creation in the precision medicine space requires a long-term view - regardless of the investment horizon - because precision medicine is not a trend but an aspiration for the very future of healthcare. Across the life sciences sector, advancements taking place over the next few years will be only milestones on the path to that ultimate destination. Successful inorganic growth strategies in the precision medicine space must therefore be built with this 10+ year strategic perspective in order to optimize value at exit.

For private equity firms investing in this market, portfolio company valuations at the end of each investment horizon depend as much on elucidation of a viable long-term strategy as they do on current enterprise value. It is vital that strategy development include roadmaps not just for current investors, but for those in future phases of the company's lifecycle. Each acquisition in the current investment horizon must still be accretive but must also be part of a longer-term strategy which will make sense to the next group of investors and demonstrate how they, in turn, will be able to realize this value with the group which comes after them.

To learn about Crosstree's Strategic Services expertise and capabilities, visit CrosstreeCapital.com.

Inorganic strategy development in this space is similar for public companies, though the investment horizon is by nature longer term, making it much less of a shift in perspective. With investors continuously entering and exiting, long-term narratives are expected. Still, each acquisition must be both logical within the framework of the long-term strategy and accretive in its own right.

SEQUENCING & TARGET PRIORITIZATION

Proper sequencing is critical to successful inorganic growth strategy development in precision medicine. After completing a capabilities gap analysis and building a viable long-term strategy, it's necessary to identify tangential acquisition targets with the correct capabilities for the next step on the growth map. The urge to "island hop" is often strong, as the precision medicine market offers a variety of attractive acquisition targets which can appear to fit perfectly into an existing gap.

In this nuanced market, however, plug-in acquisitions run a high risk of unrealized synergies and value erosion without granular knowledge of a target's capabilities and market position. In addition, because the market is so widely dispersed and largely privately held, deep market expertise is necessary to identify the right targets: for every 100 potential targets which appear to fill a capabilities gap, only 10-15 will likely align properly with most of the required blend of capabilities, geographic footprint, and infrastructure to effectively execute a given step on the strategic path.

While it may sound counterintuitive to seasoned investors, in this industry space, carefully sequenced tangential acquisitions which steadily build value into the platform over time will help the business achieve both short- and long-term objectives faster. With an expert, holistic view of the market, targets can be prioritized to maximize synergies and avoid inadvertently eroding value. Finally, knowledge of specific targets' prior transactions (completed and attempted) provides critical insight into which targets may or may not be willing to transact, saving precious time in a highly competitive space.

TARGET VALUATIONS & TRANSACTION EXECUTION

For these reasons, an expert, bottom-up analysis of all relevant players is necessary to accurately understand where a specific platform's capabilities fit into the big picture and identify gaps which must be filled in order to achieve long-term growth objectives. Only through this analysis comes a clear view of the current precision medicine market and a platform's position within it.

To learn about Crosstree's Investment Banking expertise and capabilities, visit CrosstreeCapital.com.

The nature of most potential targets (highly specialized, privately held, and lower middle market) demands deep domain expertise in order to determine an accurate valuation. A specialist financial advisor is necessary to synthesize granular knowledge of the market and individual targets, precedent transactions, and emerging trends in the space in order to arrive at an accurate valuation.

A financial advisor with both this expertise and relationships with the majority of the firms in the market can help both strategic and financial investors save time by knowing who may or may not be willing to sell. Leveraging these relationships along with well-informed valuations, specialist financial advisors are able to develop creative deal structures to increase the likelihood of success in what are typically extremely competitive bidding processes.

For founder-owned firms, which comprise many acquisition targets within precision medicine, financial returns are frequently not the most important consideration. When evaluating a potential transaction, founders look at factors such as cultural fit, degree of influence, management styles, and a whole host of other qualitative values when evaluating potential partners. Deep insights into converging market trends are remarkably powerful for building a value thesis that both informs the buyer and drives transformational outcomes. Financial advisors with these relationships and skill sets utilize this knowledge to help potential buyers position themselves most favorably, for outcomes which benefit all parties.

About Crosstree

As one of the leading investment banks in pharma services, Crosstree combines data, financial analysis, and an in-depth industry knowledge with real-world execution experience. Crosstree's consultants, advisors and bankers work with a world-class network of industry experts, executives, and investors in order to help formulate and execute the most accretive transactions possible for our clients. No other advisor has a deeper understanding of how the confluence of industry trends, market conditions, and growth opportunities will shape a company's value and strategic outcomes in the pharma services space.

Crosstree's deep expertise in pharma services, diagnostics and tools, and digital health provides an unprecedented advantage to prospective strategic partners in today's market. Because Crosstree works with such a comprehensive understanding of the pharma services industry, we can synthesize a company's capabilities, financial data, and market position to communicate a compelling value creation strategy or proposition to buyers, sellers, and other strategic partners.

Our Strategic Services team provides actionable plans and pragmatic guidance to create and realize greater value for our clients. By combining proprietary research, expert financial analysis, and industry knowledge with real-world execution expertise, Crosstree helps companies plan, evaluate, and execute viable in-organic growth strategies to achieve successful outcomes downstream.

In February 2021 Crosstree published its inaugural Innovations in Pharmaceutical Development™, a first-of-its-kind compendium of the industry's most innovative companies; a go-to resource of what is coming 2021 and beyond. Unlike other directories, this publication organizes the Pharma Services industry using Crosstree's proprietary and granular taxonomy, which helps define the industry in an easily understandable and concise way.

FIND OUT MORE

To learn more about Crosstree's Investment Banking and Strategic Services capabilities and life science expertise, visit CrosstreeCapital.com.

References

1 Aitken, Murray. "The Global Use of Medicine in 2019 and Outlook to 2023." *IQVIA Institute for Human Data Science,* 29 Jan. 2019. www.iqvia.com/insights/the-iqvia-institute/reports/the-global-use-of-medicine-in-2019-and-outlook-to-2023. Accessed 29 May 2021.

2 "The Personalized Medicine Report." *Personalized Medicine Coalition*, 2017. www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/The-Personalized-Medicine-Report1.pdf. Accessed 29 May 2021.

3 Grant, Charley. "The Side Effects of Million-Dollar Drugs." *The Wall Street Journal*, 1 Mar. 2019. www.wsj.com/articles/the-side-effects-of-million-dollar-drugs-11551447001. Accessed 29 May 2021.

4 "Precision Medicine Market - Growth, Trends, Covid-19 Impact, and Forecasts (2021 - 2026)." *Research and Markets*, 2021. www.researchandmarkets.com/reports/4520139/precision-medicine-market-growth-trends-covid. Accessed 29 May 2021.

5 "Personalized Medicine Market Size, Share & Trends Analysis Report By Product (Personalized Medical Care, Personalized Nutrition & Wellness, DTC Diagnostics, Telemedicine, Complementary Medicine), And Segment Forecasts, 2021 - 2028". *Grand View Research*, 2021. www.grandviewresearch.com/industry-analysis/personalized-medicine-market. Accessed 29 May 2021.

6 "Europe Organoids Market Forecast to 2027 - COVID-19 Impact and Regional Analysis By Type; Application; Source". *ReportLinker*, 2021. www.reportlinker.com/p06027801/Europe-Organoids-Market-Forecast-to-COVID-19-Impact-and-Regional-Analysis-By-Type-Application-Source.html. Accessed 29 May 2021.

7 "World Fact Sheet". *Global Cancer Observatory*, 2020. gco.iarc.fr/today/data/factsheets/populations/900-world-fact-sheets.pdf. Accessed 29 May 2021.

8 "Global Market Insights on Precision Medicine (2020-2026)". *UnivDatos Market Insights*, 2020. univdatos.com/report/precision-medicine-market-current-analysis-and-forecast-2020-2026. Accessed 29 May 2021.

9 "Personalized Medicine and Value Assessment Frameworks: Context, Considerations, and Next Steps". *Personalized Medicine Coalition*, 2017. www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_and_VAFs.pdf. Accessed 29 May 2021.

10 "Personalized Medicine at FDA: The Scope and Significance of Progress in 2020". *Personalized Medicine Coalition*, 2020. www.personalizedmedicinecoalition.org/Userfiles/PMC-Corporate/file/PM_at_FDA_The_Scope_Significance_of_Progress_in_2020.pdf. Accessed 29 May 2021.

11 "Personalized Medicine". *U.S. Food and Drug Administration*, 2021. www.fda.gov/medical-devices/in-vitro-diagnostics/precision-medicine. Accessed 29 May 2021.