The ability to properly address human disease has historically been constrained by an imperfect understanding of the fundamental role that genetics plays in prevention and treatment. Many serious conditions, such as cancer, strokes, and diabetes, tend to be heterogeneous in nature and can be the product of rare genetic mutations in the human genome. For example, women with BRCA1 or BRCA2 gene mutations have up to a 72% chance of having breast cancer in their lifetime versus 12% of the general female population, and a 44% risk for ovarian cancer versus 1.3%.1 Advocates of precision medicine envision a future in which all patients receive a diagnostic test to determine their susceptibility to certain diseases and drug responses based on their genetic makeup, enabling medical professionals to make more informed and cost-effective decisions. Often referred to as personalized medicine or targeted therapy, precision medicine may represent a revolutionary shift in healthcare, one that can reduce the need for guesswork, variable diagnoses, and treatments based on generalized demographics, through the greater application of genomics.

Precision medicine is transforming the pharmaceutical industry and patient care, and it has the potential to lessen the rising cost of healthcare worldwide as populations age. This point is especially salient in the United States, where the number of people over the age of 65 is expected to double from 43.1 million in 2012 to 83.7 million by 2050.2 The application of genomics across the healthcare industry has been shown to alleviate many of the inefficiencies that currently encumber the nation’s health system, such as false positive and negative test results, unnecessary prescriptions, incorrect dosages, and adverse drug reactions. Demand for personalized medicine will likely keep increasing, touching on a broad range of areas including clinical research and development (R&D), pharmaceuticals, insurance, hospitals, and direct-to-consumer applications like genetic testing kits. The growth opportunities for agriculture are also tremendous, such as the discovery of new systems to help identify crop plants that are more adaptable to climate change.3

Next-Generation Sequencing: Enabling Precision Medicine and More

The United States and United Kingdom joined forces in 1990 to launch the Human Genome Project (HGP), the first major effort of its kind to fully sequence the DNA of the entire human genome. In the years since its completion in 2003, at a cost of $1 billion, advancements in technology and automation have made it possible to sequence a genome in under an hour at a cost of $1,000 (Chart 1, page 2), providing a

---

powerful tool for scientists to explore the link between genetics and human disease. In addition, the governments of at least 12 countries have invested more than $4 billion in genomic medicine initiatives since 2013.\(^5\)

In 2018 a new gene editing tool called CRISPR-Cas9 was introduced, allowing scientists to add, eliminate, or modify defective genes that may raise one’s risk for a disease. CRISPR-Cas9 can also sequence longer genes relatively efficiently and in precise detail, uncovering blocks of DNA often missed by conventional tools. CRISPR-Cas9 is not solely tied to the healthcare industry. The technology could also help in the search for more sustainable sources of fuel and manufacturing chemicals.\(^6\) Further, the genomics market in agriculture is projected to reach $11.7 billion by 2025,\(^7\) as pressure mounts to change plant and animal breeding practices as a means of maintaining the world’s food supply in a warming environment.

The Future of Healthcare: Detection and Prevention

The advent of precision medicine aligns with the global effort to reduce the surging cost of healthcare. More people are reaching retirement age and increasingly relying on public and private healthcare benefits. This group is currently the fastest growing demographic in the United States and has a higher propensity for developing genetic diseases like cancer (median age of 66).\(^8\) Precision medicine offers a different path to treat complex diseases, reduce adverse drug reactions, and target populations for which a drug may work best.

Precision medicine uses genetic data to determine the drugs and treatments that will work best for a patient, a significant shift from the traditional trial-and-error methodology. For example, targeted therapies could lead to a significant drop in breast cancer related treatment expenses. Diagnostic testing raises the likelihood of detecting the presence of a disease before symptoms materialize, allowing for preventive measures and early intervention before it enters the advanced stages. Several private insurance providers as well as the US government now cover screening for inherited breast and ovarian cancer due to the cost savings.\(^9\) In our view, the economics of investing in the field of genomics has become significantly more attractive as patient care guidelines and insurance coverage have caught up to the scientific advances.

Pharmacogenomics: Success through Data

In 2017 the US Food & Drug Administration (FDA) green lighted the first targeted therapies for patient use, one for childhood leukemia and the other for adult lymphoma, ushering in a new era for healthcare. Since then, the FDA has worked to expedite the approval process for these type of drugs, motivated by a high rate of success in clinical trials.\(^10\) As a result,
leading pharmaceutical and biotech companies have diversified their pipelines to include gene therapy, with the global market estimated to grow to $13 billion by 2024.\textsuperscript{11} Recent momentum has also been driven by an uptick in mergers and acquisitions as cash-flush companies look for new and sustainable sources of revenue. In 2019, Roche Holding AG acquired the genomics company Spark Therapeutics, Inc., attracted by their deep pipeline that includes four gene therapy drugs in clinical trials for such ailments as hemophilia and Huntington’s disease.\textsuperscript{12} The FDA anticipates that by 2025 it will be receiving 200 new gene therapy drug applications and approving 10-20 of them a year, pointing to the more than 800 therapies already awaiting review as capital investment intensifies in the sector.\textsuperscript{13}

The National Institutes of Health (NIH) has reported that there are approximately 7,000 rare diseases affecting roughly 30 million people in the United States. Treatments exist for only a few hundred of these diseases,\textsuperscript{14} presenting a significant opportunity for innovative drug makers to gain market share. The large amount of data required for impactful R&D can be costly and time consuming to acquire, however, big data projects have become another source of market growth. For example, a number of pharmaceutical companies are funding a project with the UK Biobank to sequence 500,000 human genomes in exchange for privileged access to the information.\textsuperscript{15} In the direct to consumer sector, the popular genetics testing site 23andMe\textsuperscript{®} has analyzed the DNA of over 12 million people since 2006,\textsuperscript{16} making it one of the largest sources of genetic data worldwide, and the company has also published over 100 scientific papers.\textsuperscript{17}

**Novel Coronavirus (COVID-19) and Genomics**

The rapid spread of COVID-19 in early 2020 and the ensuing health crisis present an illustrative example of how genomics is changing the approach to healthcare. US-based Gilead Sciences, Inc. leveraged its knowledge of how similar the COVID-19 genome was to other viruses for which it had already developed a vaccine. It expedited clinical trials of remdesivir as a treatment for COVID-19, and early results look promising as of this writing. Compassionate use clauses have opened the door for already infected patients to use the drug (with a physician’s approval). Additionally, a clinical trial involving over 1,000 patients conducted by the NIH showed that patients hospitalized with COVID-19 recovered 31% faster when receiving remdesivir than patients who received a placebo.\textsuperscript{18} While clinical trials will be needed to confirm the efficacy of the drug, knowledge of the virus’s genome was the catalyst for its rapid development.

The COVID-19 genome was sequenced much faster than previous coronaviruses over the last 20 years, like severe acute respiratory syndrome and Middle East respiratory syndrome, due to advances in genomic technology. Not only can genomic data expedite clinical research of potential therapies and vaccines, but it also allows scientists to understand the origins of the virus. Specifically, research


\textsuperscript{14} National Center for Advancing Translational Sciences, “Rare Disease Day at NIH 2020,” https://ncats.nih.gov/news/events/rdd.

\textsuperscript{15} Biobank, “UK Biobank leads the way in genetics research,” https://www.ukbiobank.ac.uk/2019/09/uk-biobank-leads-the-way-in-genetics-research-to-tackle-chronic-diseases/.

\textsuperscript{16} https://mediacenter.23andme.com/company/about-us/.

\textsuperscript{17} https://www.23andme.com/publications/.

Genomics: Opportunities in Precision Medicine

supported by the NIH using genomic data showed that the virus’s sequencing data closely resemble that of bat coronavirus, and that the unique adaptations of COVID-19 most likely occurred naturally, likely from mutated proteins in bats or pangolins.¹⁹

The advance of COVID-19 from a regional epidemic to a global pandemic caught many nonvirologists off guard. However, this is the third coronavirus outbreak in the last 20 years, and in each case the various disciplines of genomics have played an increasingly larger role. Therefore, in our view, the impact of COVID-19 will likely lead to greater investment in the science of genomics, enhancing the potential investment opportunity over the long term.

Conclusion

Thematic investments normally originate from technological advancements, trends in populations, shifting consumer preferences, or changes to regional economies. However, identifying these structural shifts and the associated thematic investment opportunities can be difficult. History offers us a simple but effective road map to navigate these decisions irrespective of constant advances in technology, rapidly evolving demographic preferences, volatile political environments, or even world wars. The most successful thematic investments typically occur when the marginal cost of a new technology intersects with a structural shift or a global problem it can potentially solve. Today the convergence of innovations that began decades ago with the HGP and economies of scale driving down the costs of genome sequencing present an attractive investment opportunity in genomics and its related interdisciplines. Advances in genomics and precision medicine will likely play a central role in resolving the rapid rise of healthcare costs worldwide. Lastly, the recent global battle with COVID-19 has brought to the forefront the rapidly expanding opportunity set genomics offers researchers within the healthcare community to synthesize a virus’s genetic data and dramatically accelerate the timeline in developing drug therapies and vaccines.

Erik Casalinuovo, CFA
Director, Investment Strategy

John Ravalli
Managing Director of Portfolio Strategy

Julia C. Wirts, CFA
Investment Advisor


For more information, please contact your Hawthorn advisor.

For definitions of indexes used in this publication, please refer to pnc.com/indexdefinitions.

The PNC Financial Services Group, Inc. (“PNC”) uses the marketing name Hawthorn, PNC Family Wealth® to provide investment, wealth management, and fiduciary services through its subsidiary, PNC Bank, National Association (“PNC Bank”), which is a Member FDIC, and provides specific fiduciary and agency services through PNC Delaware Trust Company or PNC Ohio Trust Company. This report is furnished for the use of PNC and its clients and does not constitute the provision of investment advice to any person. It is not prepared with respect to the specific investment objectives, financial situation, or particular needs of any specific person. Use of this report is dependent upon the judgment and analysis applied by duly authorized investment personnel who consider a client’s individual account circumstances. Persons reading this report should consult with their PNC account representative regarding the appropriateness of investing in any securities or adopting any investment strategies discussed or recommended in this report and should understand that statements regarding future prospects may not be realized. The information contained in this report was obtained from sources deemed reliable. Such information is not guaranteed as to its accuracy, timeliness, or completeness by PNC. The information contained in this report and the opinions expressed herein are subject to change without notice. Past performance is no guarantee of future results. Neither the information in this report nor any opinion expressed herein constitutes an offer to buy or sell, nor a recommendation to buy or sell, any security or financial instrument. Accounts managed by PNC and its affiliates may take positions from time to time in securities recommended and followed by PNC affiliates. PNC does not provide legal, tax, or accounting advice unless, with respect to tax advice, PNC Bank has entered into a written tax services agreement. PNC does not provide services in any jurisdiction in which it is not authorized to conduct business. PNC Bank is not registered as a municipal advisor under the Dodd-Frank Wall Street Reform and Consumer Protection Act. Securities are not bank deposits, nor are they backed or guaranteed by PNC or any of its affiliates, and are not issued by, insured by, guaranteed by, or obligations of the FDIC, the Federal Reserve Board, or any government agency. Securities involve investment risks, including possible loss of principal.

“Hawthorn, PNC Family Wealth” is a registered service mark of The PNC Financial Services Group, Inc.

©2020 The PNC Financial Services Group, Inc. All rights reserved.