



The Core Research Series

Personalized Medicine: Research Tools Advance New Opportunities Across The Healthcare Sector

By

Daphne Karydas

Vice President
Equity Research Analyst

Karen Miki Behr

Equity Research Analyst

Introduction

The promise of personalized medicine has historically been stymied by technical challenges as the tools available were not only costly but slow and cumbersome. However, as analytical speeds increase and costs simultaneously decline, there are opportunities across the healthcare sector to capitalize on the wealth of data being produced.

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What is Personalized Medicine?

The ultimate goal of personalized medicine is to tailor medical management to an individual's unique genetic makeup, lifestyle and environment, thereby maximizing treatment efficacy and mitigating adverse events. This arrangement requires not only a comprehensive understanding of genetic differences between individuals and their correlation with disease, but also the means to interpret these differences in a clinically meaningful manner.¹

While the ideal scenario described above has not yet materialized, a few patient-specific treatments have entered the market. Herceptin, the most widely known example, is only indicated for breast cancer patients who overexpress the HER2neu receptor. The duration of Pegasys or Peg-Intron therapy can vary significantly and is dictated by the infected patient's Hepatitis C genotype (genetic variant).

Such discoveries have been more fortuitous than the result of any systematic evaluation of the genome. Therefore, the 2003 completion of the Human Genome Project was heralded as the start of a new era. With the genome map in hand, it became possible to more systematically evaluate interpatient genetic differences.

However, cost effectively analyzing and utilizing the data from the Human Genome Project proved challenging. To put this undertaking in perspective, it took several labs working in concert for nearly 15 years at the cost of \$3 billion to map the human genome; despite this, no major breakthrough in drug development has materialized as a direct result of the project. Since then, research tools have evolved, making research much simpler and cheaper. Specifically, microarray technology and, more recently, next generation sequencers have made more widespread genome screening, sequencing/resequencing, and expression profiling feasible. These breakthroughs have led to an exponential growth in the number of genomes sequenced and genes identified.

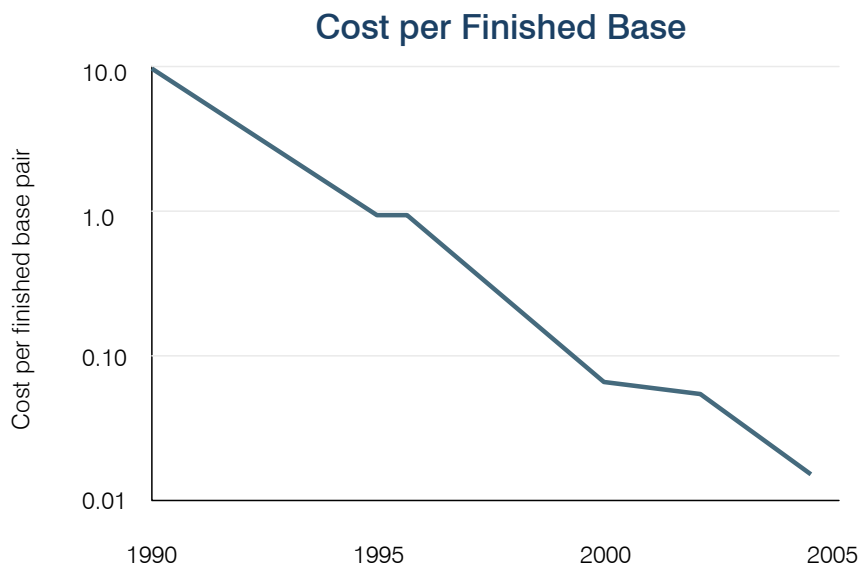
¹ Lee C et al. Structural genomic variation and personalized medicine. NEJM. Feb 2008

Speeding to Discovery

Although neither microarrays nor automated sequencing devices are new, recent advancements have radically increased throughput while simultaneously lowering costs.

For example, microarrays are now capable of interrogating millions (to billions) of genetic data points on a single microscope-sized slide. Driven by data generated through publicly funded projects, (i.e., HapMap, etc.), microarray manufacturers now have both the genetic information and technological understanding required to evaluate an entire genome. Whole genome SNP microarrays were developed to help researchers efficiently identify aberrant genetic regions; while whole genome microarrays cannot pinpoint the specific gene or mutation responsible for a disease, they can flag areas of interest. Lower density targeted microarrays and/or sequencing tools can then be used to focus on the identified region. The availability of whole genome microarrays alone (note there are many other microarray applications) has led to an explosion of research (i.e., genome wide association studies), which are attempting to link genetic differences to specific diseases.

Figure 1

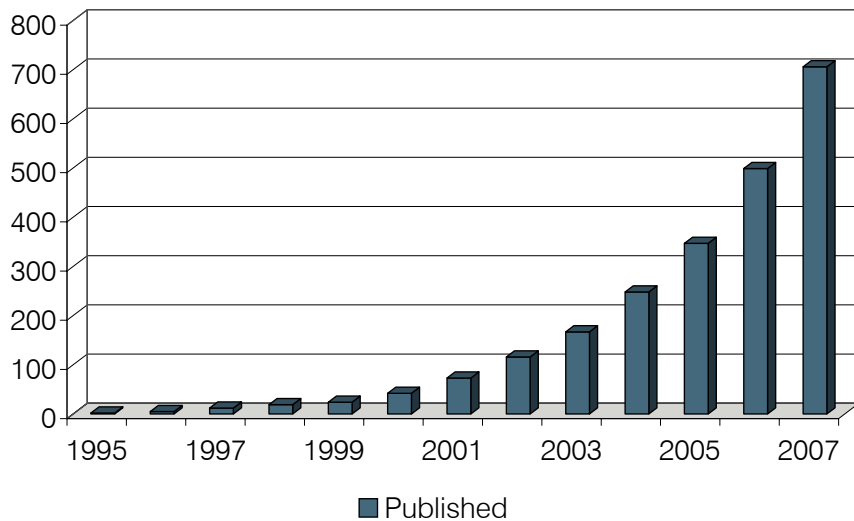


Source: R. Service. Science. 2006.

Sequencing tools have advanced significantly as well. Cheaper and faster, current next generation sequencers look close to meeting the National Human Genome Research Institute’s (NHGRI) \$100K per genome goal. This development is a significant reduction from the \$3 billion dollars associated with mapping the first human genome. Furthermore, sequencers in development are utilizing technologies capable of reducing the per genome sequencing cost to NHGRI’s next goal of \$1K. Should costs fall to the \$1K mark, researchers could use sequencing to screen for disease associated genetic abnormalities. But even at today’s costs, researchers have been able to expand the tool’s utility. From expression analysis and CHIP-Seq assessments to targeted resequencing, next generation sequencers are able to utilize speed and lower costs to aid in more targeted research.

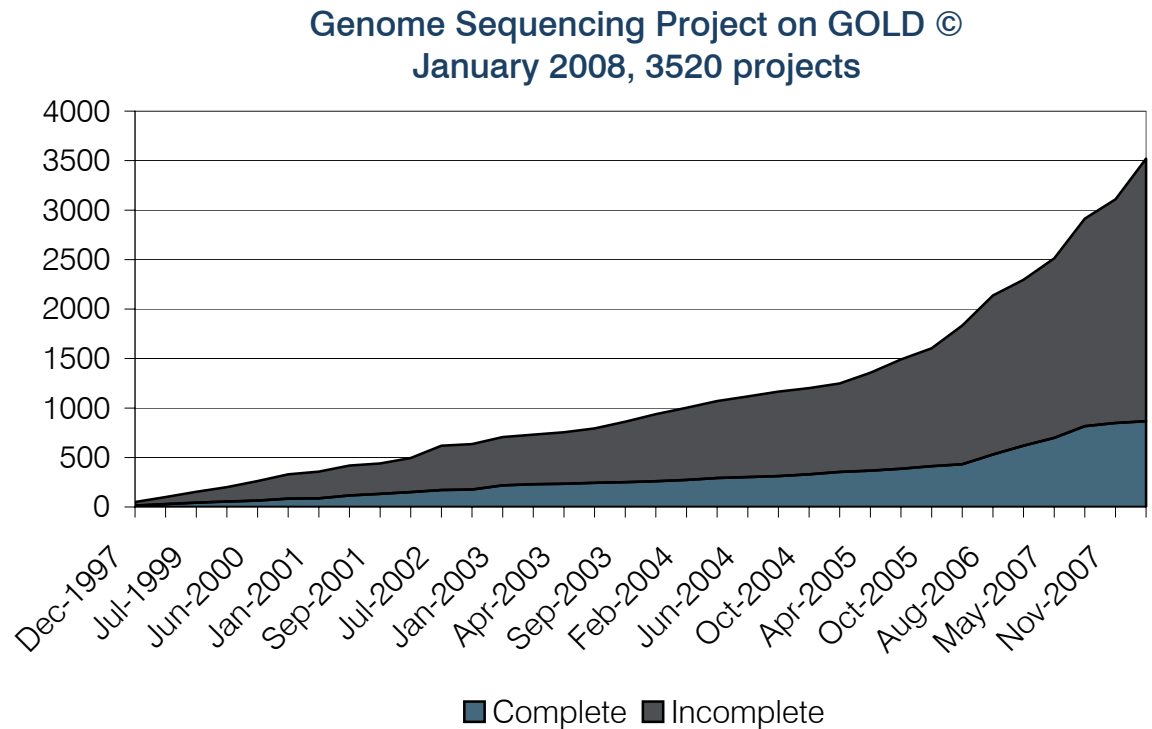
Figure 2

**Completely Sequenced Genomes ©
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Source: Genomes OnLine Database

Figure 3



Source: Genomes OnLine Database

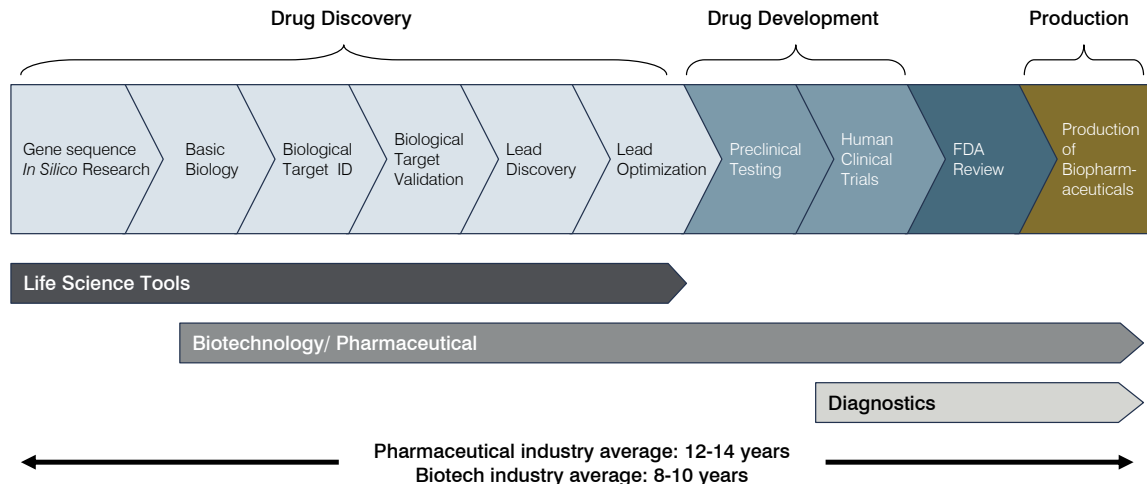
Bench to Bedside

What exactly does this mean? Where are we within the horizon of possibilities and what does this mean from an investment perspective?

Starting with the latter question, the age of personalized medicine is only just dawning. The diagram at the top of the next page outlines the steps from gene sequencing to therapeutic launch. Although there is activity throughout the development chain, life science tool improvements are primarily benefiting drug discovery today. By increasing analytical processing speed and decreasing costs, microarrays and next generation sequencers are generating more de novo (never before sequenced) genetic sequences, identifying areas of intrapopulation differences associated with afflicted patient groups, and pinpointing potential targets for drug development. Life science tools companies are also seeing a broadening of their consumer base; the decreasing costs have enabled smaller and increasingly non-academic (e.g., agricultural, etc.) labs to incorporate these tools into their research.

Figure 4

Process from Drug Discovery to Treatment Production



Source: Leerink Swann, TBCAM

All of the above suggest that a growing body of attractive biological targets will filter down the development chain. This will have clear implications for biotech and pharma. Seeking new compounds to fill their early pipeline, these companies are actively evaluating this body of research. However, the time from target identification to lead (treatment) development is quite long; as such, this will have limited near-term impact.

Therapies emerging from genetic analysis tools will likely require diagnostics to identify appropriate treatable populations. Diagnostic companies are already developing or have developed molecular diagnostics platforms. These platforms have thus far been targeted at diagnosis (e.g., rapid identification of HIV, Hepatitis C, bacterial infections, etc.), but will soon be capable of running companion assays. While applications exist today, much of the value will be unlocked when companion diagnostics and their corresponding targeted therapies come to market.

To answer the first question: ultimately, if the promise of personalized medicine holds true, these developments will reduce costs at the hospital and insurer level. The hope is that targeted therapy will prove more efficacious and less toxic than current non-specific treatments; today's drugs can work in less than 50% of patients with treatment-associated adverse events accounting for 6.5% of hospital admissions.² However, the full impact of these cost-savings remains even further out.

² Pirmohamed M et al. *BMJ*. 2004; 329:15-19

The wealth of new targets increases the likelihood that pharma and biotech will identify effective therapeutics and potentially enhance the productivity of R&D budgets.

Challenges and Concerns

Tool obsolescence: With the rapidly evolving nature of the life science tools sector, there is a very real possibility of tool obsolescence. In light of this situation, two key factors will be critical to protect corporate interests: breadth and depth of IP and tool portfolio flexibility and investment. Companies with limited patent protection and/or tool portfolios will be less likely to remain successful over the coming years.

Loss of the blockbuster drug: From its initial conception, many feared that the era of personalized medicine would mark the waning days of blockbuster drugs. However, we expect the current surge of data to be a net positive for pharma and biotech. The wealth of new targets increases the likelihood that pharma and biotech will identify effective therapeutics and potentially enhance the productivity of R&D budgets. Furthermore, when they do become available, more efficient, targeted medicines should be able to capture pricing reflective of their overall value proposition; specifically, such treatments will be capable of lowering overall healthcare costs by directly treating the disease, reducing treatment related adverse outcomes, and will, from the outset, be limited to patients who will actually benefit. Given that currently available targeted therapies are multi-billion drugs it is clear that personalized medicine is not incongruous with blockbuster drugs.

Diagnostic relevance: With potential targets identified and faster regulatory paths, diagnostics may advance ahead of treatments. These diagnostics will be of limited therapeutic and financial value until associated therapies or management protocols are developed.

As an example, Cytochrome P450 is an enzyme central to the metabolism of over thirty drugs (e.g., warfarin, certain antidepressants, proton pump inhibitors, etc.). It was discovered that Cytochrome P450 genetic variations can lead some individuals to process drugs too slowly; this leads to a gradual build up of the drug and consequently adverse events. A test has become available which can determine a patient's CYP450 genotype (genetic variant). Still, the test has been of limited value. Current treatment protocols dictate slow treatment titration and simultaneous blood monitoring to manage these known risks. The test alone will not change the way patients are managed. Until better protocols or genotype specific treatments become available, this test will add minimal societal or financial value.

Conclusion

While the age of personalized medicine is not within our immediate grasp, these advances have certainly brought it closer to reality. Over the near-term we expect tools companies to continue to benefit from the surge of interest in genetic research. In the mid-to long-term timeframes, we expect both diagnostics and pharma/biotech be the beneficiaries. The age of personalized medicine is here. Be patient and buckle in. We're in for a long, interesting ride.

Author Biographies

Daphne Karydas

Vice President

Daphne is an Equity Research Analyst on The Boston Company's Core Research Team covering the healthcare sector.

Prior to joining The Boston Company, Daphne was an Analyst at Goldman Sachs covering the healthcare sector. Before that role, Daphne worked in the Investment Banking Division of Goldman. Prior to joining Goldman Sachs, Daphne was a Project Chemical Engineer at Merck & Company.

Daphne earned a BA and an MS from Massachusetts Institute of Technology, and an MBA from Harvard Business School. Daphne is a Level II candidate in the Chartered Financial Analyst Program.

Karen Miki Behr

Miki is a Research Analyst on The Boston Company's Core Research Team covering the healthcare sector.

Prior to joining The Boston Company, Miki was an Engagement Manager at Leerink Swann Strategic Advisors (formerly MEDACorp Corporate Consulting) evaluating strategic growth opportunities for Pharmaceutical, Biotech, Medical Device and Private Equity clients.

Miki earned a BA in Molecular and Cell Biology from the University of California, Berkeley and holds a MBA from MIT Sloan School of Management.

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