SUMMARY
The growth of precision medicine coupled with advances in technological and scientific approaches means that more research opportunities for the pharmaceutical industry are bound to emerge. However, it has to be recognized that this is a new R&D paradigm that will require the industry to be proactive in adapting and optimizing its use of new datasets.
In his 2015 State of the Union address, President Barack Obama announced the intention to launch a Precision Medicine Initiative with the ambitious goal of enabling the identification of the right treatment for any given patient (1). The huge research initiative launched in 2016—yet another sign of the growing interest and increasing opportunities in precision medicine.

THE GROWTH OF PRECISION MEDICINE

The drug that can be considered the first precision medicine entered the market in 1998, at a time when the concept was referred to as personalized medicine. Herceptin (trastuzumab) was first used for the treatment of a subgroup of breast cancer patients with human epidermal growth factor receptor 2-positive (HER2+) tumors.

Following the completion of the Human Genome Project in 2003, precision medicine has expanded to the point where it is possible to match certain patients to tailored treatments via diagnostic tests based on the presence (or absence) of biomarkers. Such an approach promises better clinical outcomes, safer medicines and less wastage. In theory, the healthcare system will also benefit, since treatments will only be directed to those who will benefit most, resulting in an economic advantage if medical resources are scarce (2).

The fundamental concept of precision medicine is treating the right patient at the right time with the right therapy. As pointed out by the PHG Foundation (Foundation for Genomics and Population Health) in a recent position paper (3), this is actually the main objective of all medicine. The precision medicine approach and related advances in medical technology have given clinicians the ability to use genetic information together with lifestyle and environmental data to refine both diagnostic and treatment choices.

For these reasons, and alongside the increasing demand to provide value to healthcare systems, drug developers have begun to move away from the dominant one-size-fits-all blockbuster approach. In the words of The Journal of Precision Medicine, the pharmaceutical industry has "embraced personalized medicine, despite the absence of a tried-and-tested business model that ensures success" (2).

Indeed, most companies now report biomarker strategies in R&D aiming to refine drug targets and segment patient populations. According to the Tufts University Center for the Study of Drug Development, more than 40 percent of all drugs in development have the potential to be personalized medicines, and this figure is predicted to increase to almost 70 percent over the next five years (4).
The concerted interest in precision medicine has translated into an increasing number of such drugs being approved by the US Food and Drug Administration (FDA). In 2015, 28 percent of drugs approved by the FDA were precision medicines, up from 22 percent in 2014 (2). According to the Personalized Medicine Coalition, such drugs “are becoming a larger portion of available new drugs […] Personalized medicine is rapidly coming of age” (5).

However, the rapid expansion of precision medicine raises the issue of how fit-for-purpose the traditional R&D model is in this new paradigm. The industry has begun to adapt, as seen in the selection of subjects based on biomarker information and an increase in the number of accelerated approvals based on striking results from early-phase clinical trials. However, a more determined effort will be required if the industry is to be prepared for the emergence of precision medicine in every disease area, including specifically individualized treatments and how to optimize the use of big data. The latter is particularly important with the increase in the amount of genomics, health and lifestyle information that will have to be taken into account.

MORE RESEARCH NEEDED

The advances in precision medicine over the past few years have been impressive, as dramatic advances in science and technology have accelerated knowledge of the biological mechanisms of disease. However, there are still many conditions for which the specific biomarkers of disease and the underlying pathways are unknown. This presents situations where pharmaceutical companies are forced to delay a diagnostic biomarker approach, choose a test that is still under development, or use novel biomarkers that are not fully understood. This can severely limit the efficiency of drug development.

As such, it is essential that the industry be proactive. “This can be achieved by taking advantage of new tools and scientific advances in order to focus on research around disease mechanism and to gain a better understanding of biology at a molecular level,” says Will Chen, Vice President Product Management and Business Development, Precision Medicine, at Elsevier. This research effort will need to focus beyond biomarkers that just establish drug targets to biomarkers that also define diseases, predict the drug response and identify disease risk and prognosis. Detailed disease networks at a molecular level should also be a critical research focus.

Several excellent research initiatives are taking the newest science and turning it into usable outcomes. One example in the UK is the University of Manchester’s £22 million Stoller Biomarker Discovery Centre, which opened in June and was developed in partnership with life-sciences technologies firm SCIEX. The Stoller Centre aims to accelerate biomarker identification for disease risk, diagnosis, response to therapy and prognosis for indications including cancer, psoriasis, kidney disease and arthritis. This is achieved using advanced approaches such as proteomics and health informatics.

For instance, proteomics is being explored to analyze proteins in women’s blood samples to define potential biomarkers of the risk of ovarian cancer, because this technique provides more information about the pathogenesis of ovarian cancer and possible mechanism of drug resistance than sequencing or microarrays and therefore has high potential for the development of biomarkers for early detection (6).
Another project is the US government’s Precision Medicine Initiative (PMI), announced in 2015 and funded with an initial investment of $215 million (1). The National Institutes of Health (NIH) recognizes that the term precision medicine is relatively new, although “the concept has been a part of healthcare for many years” (7) and is “an emerging approach for disease treatment and prevention that takes into account individual variability in genes, environment, and lifestyle for each person.” This approach will allow doctors and researchers to leverage advances in genomics and other technologies to better predict the outcome treatment and prevention strategies for a particular disease in a given groups of people, sharply contrasting with the one-size-fits-all approach, in which disease treatment and prevention strategies are developed with less consideration of individual biological and lifestyle differences (7).

The initiative is also building on precision medicine’s success in oncology, to extend into other disease areas, such as diabetes, heart disease, Alzheimer’s, obesity, mental illness and rare diseases. This will be achieved through the creation of a research cohort of at least 1 million Americans who will voluntarily share their data. It will consider individual differences in environment, genes and lifestyle, and link them with electronic health records. Christopher Austin, director of the National Center for Advancing Translational Sciences at the NIH, which is leading the PMI, calls this approach to research “atypical” but says this sort of collaboration with participants will become the norm.
It is significant to note that the main thrust of such initiatives is taking place outside of big pharma, “reflecting the fact that pharma has reduced much of its investment in early-stage research,” says Chen, “focusing instead on late-phase clinical development, sales and marketing.” To fill their pipelines, pharma companies have to “buy-in” drug candidates from academia or biotech start-ups that have already discovered and researched the molecules. By doing so, companies reduce their risk, but the result, says Chen, is that “companies take drugs into development without an understanding of the mechanism of action or an understanding of the disease itself, creating a knowledge gap and potentially increasing the chance of trial failure.”

There have been efforts to rectify this along with concerted focus on specific therapy areas, but Chen says more still needs to be done: “Companies do need to focus on research more and have more confidence in the biology.” Indeed, this becomes increasingly important as science now allows old drugs to become more efficacious and failed drugs to be rescued through a biomarker approach.

THE BENEFITS OF UNDERSTANDING BIOLOGY

The benefits of applying a robust and well-researched biomarker approach are evident. Bristol-Myers Squibb (BMS) felt this keenly when it took the risk of not using a biomarker approach for its immuno-oncology drug Opdivo in trials for first-line treatment of non-small cell lung cancer. Results showed that Opdivo failed to slow tumor growth in previously untreated patients, and the company’s shares dropped 16 percent. By comparison, Merck was trialing the immuno-oncology drug Keytruda in the same indication, but chose to limit the trial population to patients with high levels of the PD-L1 biomarker, knowing they were likely to benefit from the drug. As a result, Keytruda was found to extend the lives of patients. Says Chen: “There is speculation that if BMS had looked specifically at PD-L1, it would have been more likely to succeed.”

A report early in 2016 from Amplion, BIO and BioMedTracker, examined 10,000 clinical trials, found that those drugs developed with a biomarker program—selecting patients more likely to respond to the drug—were three times more likely to reach regulatory approval (8). AstraZeneca reviewed hundreds of its compounds and found that when it had a good understanding and confidence in the biological role of the target and incorporated genetic information, compounds were more successful through phase II trials (9). Pfizer’s Xalkori (crizotinib), an oral small-molecule that targets the ALK, MET and ROS1 tyrosine kinases showed spectacular median response rates (between 50 percent and 60 percent) in two single-arm trials with a total of 255 patients with ALK-positive non-small cell lung cancer (NSCLC). These results led to accelerated FDA approval of Xalkori in 2011 (10). As Chen says, “Having these biomarkers is important.”

“For precision medicine to meet its promise of improved efficiency, it requires a database to identify the right patients”

Will Chen, Vice President Precision Medicine, at Elsevier
DATA TIDAL WAVE

The data from genetic and related biomarker research is just the tip of the iceberg in the evolutionary path of precision medicine. As science advances through the omic disciplines, electronic health records, computational biology and the capture of lifestyle and environmental data, there will be a tidal wave of new information with the potential to advance precision medicine toward truly individualized treatments. This more holistic approach is the basis of the Precision Medicine Initiative in the US.

In just five to ten years, people could be routinely paying for genetic screening and genome sequencing. Chen believes these findings will sit alongside data collected from wearable devices that self-track diagnostic data and lifestyle factors. All this information will be linked with electronic health records, providing an abundance of personalized health data.

“The advantages of such a situation present a new opportunity for research, where combining genomic data with digital tools will help deliver precision medicine,” says Chen. For instance, such information could be pooled to treat patients more efficiently, essentially by referring to efficacy results from patients of a similar profile. Such a database could also be utilized for clinical trial recruitment and analyzed for drug response, which could continuously refine R&D retrospectively. “For precision medicine to meet its promise of reduced clinical trial costs and improved efficiency, it requires a database to identify the right patients and where those patients are located,” says Chen.

“The pharmaceutical industry needs to be ready for this and willing to collaborate.

Besides the obvious operational challenges of access to data and integration of information from multiple sources, there are many challenges that the big data environment will present to the pharmaceutical industry, not least the need for new skills—such as bioinformatics—and the appetite to collaborate with new and emerging entrants to the healthcare space, such as the technology giants from Silicon Valley and beyond. The domino effects of the big data revolution on clinical trials and business strategy will be significant.

These reasons compel pharma to take stock of the new research paradigm. As yet, the industry is not taking full advantage of the early research opportunities presented by the new science and technology, or the currently available data, in order to move the precision medicine agenda forward. The vast quantity of data that is set to become available will require a concerted top-down commitment in adapting the way the industry does research and who it collaborates with. It is fundamental that the pharmaceutical industry prepares now—for the advance of science shows no signs of abating.
REFERENCES


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