By Taren Grom

Biotechnology Companies

Innovation and technology remain key assets of the biotechnology industry, which is moving toward value-based healthcare and patient centricity.

As the world marks the 60th anniversary of the publication of James Watson and Francis Crick's landmark work on the structure of DNA, G. Steven Burrill, CEO of Burrill & Company, notes that the industry is on the cusp of whole genome sequencing becoming a standard part of clinical practice.

"New targeted therapies are delivering on an era of precision medicine," he says. "And, the convergence of information technology within healthcare is leading to new tools that will not only create great savings by changing the way healthcare is accessed and delivered, but also empower people to take control over their own health and wellness.

"The growing middle class around the world and the rise of emerging economies are creating new demand for not just healthcare, but food, fuel, and manufactured goods," he continues. "We are faced with great challenges, but the biotech industry is forging answers."

In his recent book, Biotech 2013 Life Sciences: Capturing Value, Mr. Burrill examines the developments in the life-sciences industry during the past year and points to what's ahead. It covers the industry's breadth, from healthcare to biogreentech and discovery to delivery, while also exploring the intersection of the industry with science, policy, and society. The book can be ordered at burrillmedia.com.

JEREMY BENDER, PH.D.
Chief Business Officer
Sutro Biopharm

Advances in our understanding of the mechanisms underlying human disease continue to broaden opportunities to develop breakthrough protein therapeutics. Fully realizing these opportunities, however, will require using new technologies to rapidly interrogate the relationships between structure and biological activity, allowing for the identification, selection and development of optimized, homogeneous drug candidates.

Recent trends in the field of antibody-drug conjugates (ADCs) illustrate these opportunities. Clinical results for two recently approved products, Genentech's Kadcyla and Seattle Genetics' Adcetris, demonstrate that ADCs can provide significant clinical benefits to patients. To fully realize the opportunity that ADCs present will require next-generation agents in which all key product attributes are optimized, including antibody stability and specificity, payload activity, linker design, and the site(s) of linker/payload conjugation. However, developing such optimized products using conventional cell-based expression systems and conjugation technologies within commercially viable timeframes is not feasible. Cell-free protein synthesis technology overcomes these limitations by enabling the generation, identification, and systematic evaluation of hundreds of site-specific ADC variants in weeks, thereby allowing the selection of ADCs with optimized efficacy and safety properties. This technology can be easily scaled up, and is also being applied to the development of other protein classes, including bispecific antibodies, therapeutic peptides, and vaccines.

Interest in developing targeted therapeutics, such as ADCs and bispecific antibodies, has surged in the biotechnology industry, and the use of novel technologies, such as a cell-free protein synthesis system, will enable the rapid development of best-in-class therapeutics of these types.

MARK CORRIGAN, M.D.
CEO
Zalicus Inc.

For decades large pharma was the source for innovative new drugs but the emphasis has been shifting in the recent years as large pharma R&D budgets and infrastructure are systematically being reduced in scope. This is the broadest opportunity for the biotech industry. Today, large pharma looks to two main external sources to fuel their drug pipelines with the hopes of producing innovative new drugs of the future: biotech companies and academia. As pharma R&D budgets have been squeezed, there has been a corresponding uptick in biotech M&A and academic alliances by the pharma industry such as the Roche Genentech UCSF research alliance or the Novartis relationship with the Broad Institute.

The opportunity for the industry is captured in biotech companies bringing an urgency and directness to both the discovery and early development of their molecules. Biotech companies operate close to the financial edge — depending on early clinical success or translational research for their continued existence, this is a culture and motivation that cannot be replicated within the walls of big pharma.

While the culture and incentives within academia do not typically support the type of risk taking necessary to advance individual molecules into development on their own, universities serve to provide important molecular insights for drug targets. True innovation will come from those companies that have the foresight to recognize academic discoveries early on and apply a small-scale industrial approach to develop them.

Increasingly, the focus of drug discovery and development efforts is moving toward indications with smaller patient populations. This trend toward orphan disease indications is being driven primarily by two factors: the most significant of which is financial. The second factor is the advancement of scientific knowledge. Products developed for rare or orphan diseases typically have much more generous reimbursement models without the arduous managed care hurdles that have made it increasingly difficult for products in certain disease indications to succeed. In addition, the commercial infrastructure necessary to actively market and sell a broad-based, PC-based drug is a barrier to entry to all but the largest of companies.

Indications being pursued less are going to be

widespread diseases where there are existing therapies with acceptable risk to benefit ratios, for example hypertension and birth control, while drugs that target diseases of the aging, such as neurodegenerative disease, arthritis-based disease, and non-opioid based approaches to treating pain, are likely to lead to increased and ongoing investment in therapeutics. Unfortunately, this leaves existing diseases for which there are limited to no effective therapeutic options but for which the regulatory and commercial hurdles are so difficult that drug development is sparse to none, for example stroke, and increasingly diabetes.

The biggest challenges faced are financial and regulatory. We need increased investment in small, early-stage companies — the source of innovative therapeutics of the future. Secondly, we need to shift to a less risk adverse regulatory/approval system with fewer patients required for drug approvals, perhaps creating provisional approvals with further safety data collection ongoing during the first year(s) in the marketplace. We need to continue to tap academia as a source of important scientific breakthroughs on mechanisms of disease and not look to them to build drug development capabilities. And finally, the ultimate economic benefit of discovering and developing truly innovative drugs has to be preserved with a less restrictive pricing environment across all disease indications.

INGMAR HOERR, PH.D.
Co-Founder and CEO
CureVac

RNA is an important class of biomolecules in nature comprising many members with different functions. Messenger (m)RNAs, carriers of genetic information that are translated into protein products, are resourceful, nontoxic molecules and may be able to address the shortcomings of many therapeutic approaches. For many years, it was generally accepted that mRNAs were too unstable and too difficult to manipulate to be efficiently used as therapeutics. Recently, however, researchers faced this challenge and explored new approaches to utilize mRNAs as treatment option for human diseases. Currently, mRNAs are being developed as an entirely new class of drugs with wide-ranging potential applications, including cancer immunotherapies, prophylactic vaccines for infectious diseases and, more recently, as a promising alternative to DNA-based procedures such as therapeutic gene products and protein replacement therapies.

mRNA-based therapeutics can be synthesized to encode any protein and are broadly applicable while at the same time inherently safe because they don't need a vehicle, such as a virus, for their delivery into the cells. In fact, the first clinical trials of mRNA-based therapeutics in prostate cancer and lung cancer have shown efficacy and safety. These mRNA-based immunotherapeutics are injected directly into the skin (intradermally) and taken up by antigen-presenting cells, such as dendritic cells; they then induce an immune response to the corresponding antigen.

The speed, efficiency and lower cost of the production of mRNA-based therapeutics have come to the attention of the biotech and pharmaceutical community, and this universal biomolecule has finally made its way into clinical development. mRNA-based therapeutics are currently being investigated as transformative treatment options across a broad range of human diseases and disorders.

MIKE SHERMAN
Chief Financial Officer
Endocyte

There has been a surge in interest in developing companion diagnostics, particularly in oncology, which identify patients who will likely respond to a targeted treatment, due to their numerous benefits. The biopharma industry, as well as the FDA and EMA, have embraced the development of these tests, as they enable the development of safer and more effective drugs. Now, the benefits of incorporating these diagnostic tools even earlier in the development process are being recognized.

The most obvious benefit of the use of companion diagnostics is the reduction in clinical risk, as only patients most likely to benefit from treatment receive therapy. This can translate into smaller trials, saving both development cost and time. The efficacy benefit is also likely to be greater in the targeted patient population, which enhances likelihood of regulatory approval and improves the outlook for reimbursement. Not all firms have the diagnostic and therapeutic capability under one roof, but where they do, it can streamline the coordination of development timelines and increase likelihood of timely success.

There are more subtle benefits to be realized through earlier use of companion imaging diagnostics in development. Even as early as preclinical development, imaging diagnostics can be used to anticipate the trafficking of a potential therapeutic. So before any resources are deployed for therapeutic drug development, researchers can confirm the prevalence and specificity of the target for the drug, providing insight into both efficacy and safety. So beyond the more obvious benefit to selecting the right patients, researchers can confirm early in the process they have a viable target that's relevant for the specific indication being evaluated. The use of an imaging technology further enhances that value as it provides a full-body, non-invasive view of the target. This is important in light of recent findings that tumor characteristics can change over time and differ within the same patient across their disease.

RON SQUARER
CEO
Array BioPharma

We believe the biggest opportunity in biopharma today is to pursue development of new drugs in disease sub-populations based on patient selection markers. By identifying populations of patients based on the underlying biology of both the disease and the drug mechanism, biotechnology companies can accelerate development timelines; enhance clinical activity; and better position their products at launch in the minds of prescribers.

While patient selection markers have been positioned typically as those that identify patients more likely to respond to a drug, it is just as important to identify markers that will help eliminate patients from the treatment pool. In a practical sense, this is important because it allows these patients the opportunity to pursue treatment with other options, on which they may have a greater chance of achieving clinical benefit.

We've assigned a very high priority to the identification of biomarkers to drive patient selection in our research and development efforts, and this investment is bearing fruit. Currently, we have two Array-invented MEK inhibitors — partnered with Novartis and AstraZeneca — progressing into five planned registration trials in patient populations selected based on Ras-Raf-MEK-Erk pathway mutations.

By focusing on potential target populations, we believe we can enhance our clinical activity, improve the speed at which our trials will enroll, and ultimately improve the likelihood that regulatory agencies will look favorably on our ability to match drug effect with patients most likely to respond.

This trend is accelerating across the industry, as drug development companies are finding innovative ways to accelerate development times, reduce time to market, and get drugs to patients quicker by very precisely targeting subpopulations who will respond to their drugs. We believe this is one of the most important and impactful trends in the drug development industry today. PV