Bio Platforms, Featured Articles, Formulation Development

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DNA VACCINES MARKET – DNA Vaccines: Strategic Markets & Emerging Technologies

INTRODUCTION

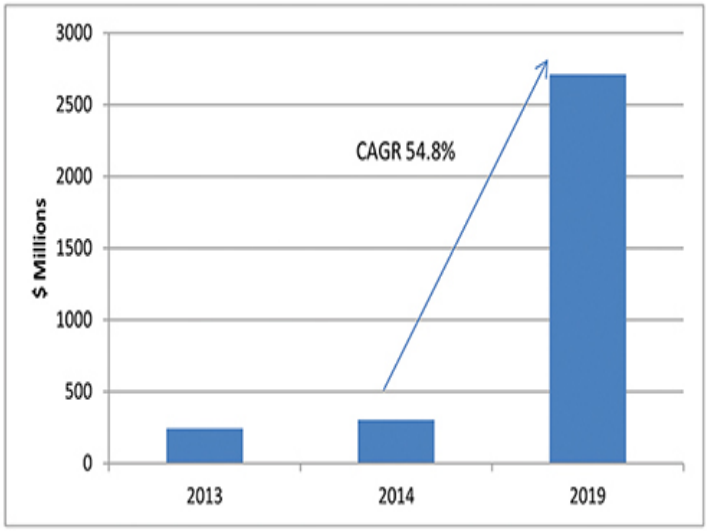
The vaccine industry is rapidly changing from a mostly empirical approach to one based on rational design. Rapid developments in molecular biology, DNA synthesis, and immunobiology enable rational design approaches. These technologies allow highly targeted vaccines aimed at specific epitopes. The result is new vaccines for a wider range of diseases than was previously feasible, including a new class of therapeutic vaccines. These new technologies allow pharmaceutical firms to discover and develop high-value vaccines for novel applications, creating a substantial new market opportunity.

DNA vaccines have many potential advantages, including specific targeting, use of multiple genes to enhance immunity, and reduced risk compared with conventional vaccines. Translating the advantages of DNA vaccines into the clinic has historically been difficult; however, new advances in the fields of vaccine design and DNA delivery are addressing previous issues. Achievements in these fields promise to overcome the translational hurdles and create strategic opportunity.

According to BCC Research (www.bccresearch.com), the global market for DNA vaccines is estimated at $305.3 million for 2014 and is forecast to grow at a stellar 54.8% compound annual growth rate (CAGR) to reach $2.7 billion by 2019. High growth during this period is a combination of a low starting base and forecasted introduction of several DNA vaccines late in the forecast period. While research tools and animal health clinical applications dominate the market today, by 2019 human clinical DNA vaccines will make up the vast majority of this market.

FIGURE 1

Global Value of DNA Vaccine Market



Source: BCC Research (BIO067B), July 2014

DNA VACCINES

The first DNA vaccine to be approved was the equine West Nile virus vaccine in 2005. This approval validated the DNA vaccine model in non-humans, and since then, the model has been validated in clinical trials in humans.

In 2006, Merck (together with its European partner, Sanofi Pasteur) launched its cervical cancer vaccine, Gardasil. The success of this vaccine, and its second-in-line competitor, Cervarix (GSK), marked a milestone in the vaccine industry. The products competed in an entirely new vaccine market for prevention of a specific cancer, precancerous genital lesions, and genital warts

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INDUSTRY EVENTS

BIO 2020
June 8-11, 2020, San Diego, CA

BIO CEO & Investor Conference
February 10-11, 2020, New York City

CPhI North America
May 5-7, 2020, Philadelphia, PA

Drug Delivery Partnerships Meeting
March 30-April 1, 2020, Orlando, FL

Drug Development Networking Summit & Table-Top Exhibition
April 16, 2020 – Bridgewater Marriott, Bridgewater, NJ

INTERPHEX
April 28-30, 2020, New York City

PDA Annual Meeting
March 30-April 1, 2020, Raleigh, NC

due to the human papillomavirus (HPV). These products provide blockbuster potential for their developers and change the way vaccines are marketed and distributed.

DNA vaccines arise from a simple concept – the coding sequence for a pathogenic antigen is incorporated into a pDNA, and the sequence is then expressed in the host cell. Because DNA vaccines do not use a pathogen itself or pathogenic protein, there is no need to prepare, purify, or deliver a pathogen or protein. This is a key advantage of DNA vaccines and one reason for their growing use in vaccine development programs.

DNA vaccines target a wide range of traditional pharmaceutical markets, such as cancers and allergies, as well as infectious diseases. The greater vaccine industry has proven that it can generate products with non-traditional applications and blockbuster potential, with the introduction of Gardasil by Merck. DNA vaccines are poised to follow this emerging model to generate significant future market potential.

New biotechnologies and nanotechnologies are driving DNA vaccine development. Particularly important to DNA vaccines reaching their potential are emerging delivery technologies, such as electroporation (EP), innovative vaccine formats such as DNA prime-adenovector boost, and novel molecular adjuvant technologies. These technologies are providing the means for achieving higher efficacy in humans.

DNA vaccines have already made significant progress to date. Nearly 100 clinical trials are underway in humans for a wide range of diseases, and there is a deep pipeline of preclinical projects. A small but strategic market segment is commercial today, including research tools and animal health applications.

STRATEGIC MARKETS

Research tools and animal health represent strategic markets for DNA vaccines. These market segments play a vital role in the development of the large, human vaccine applications in two ways: they provide current good manufacturing practice- (cGMP) grade pDNA to the industry to support the vast number of clinical trials now ongoing, and they demonstrate proof of principle for DNA vaccine safety and efficacy in animals.

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RDD (Respiratory Drug Delivery)
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- Vetter Pharma International
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Human clinical DNA vaccines represent the primary future market opportunity for this industry. The momentum for commercialization of a human DNA vaccine is growing due to the inherent advantages of DNA vaccines over other vaccine formats, amid an emerging consensus within the vaccine industry that DNA vaccines are safe and efficacious in humans.

Advanced formulation strategies, including combination vaccines (eg, DNA prime followed by viral vector/peptide/recombinant protein boosts), innovative delivery methods (eg, EP), and novel adjuvants (eg, DNA sequences encoding mutant cytokines) are proving their safety and efficacy in early and mid-stage clinical trials.

Cancer is a serious worldwide health threat, particularly in developed countries, where the populations are aging and disease is prevalent. For many cancers, there are significant unmet medical needs, resulting in high mortality rates. DNA vaccines targeted against these cancers are particularly attractive market segments. Clinical trials for DNA vaccines to treat several of these cancers, including metastatic melanoma, prostate, and pancreatic cancer, and other solid tumors, are showing promising results. These vaccines will follow the new vaccine market model of blockbuster cancer vaccines recently introduced – Gardasil and Cervarix – during their commercial introduction phase.

Biotechnology tools to produce, manipulate, and purify DNA are now standard in most laboratories. The means to discover and develop new pDNA vaccines are readily available to a large cross-section of scientists. Conventional vaccine approaches have not succeeded for a large proportion of infectious diseases, and have made only slow progress in treating cancers. As a result, there are still significant unmet medical needs in these disease areas. DNA vaccines may be able to meet these needs because they use immunological pathways that are not easily achieved by other technologies.

With the recent outbreak of the pandemic swine flu virus, it is apparent that there is an increasing need to protect against rapidly mutating pathogens. Viruses that change rapidly cause emerging infectious diseases as well as established diseases, such as influenza, SARS, acquired immunodeficiency syndrome (AIDS), and West

Nile virus. There is an ongoing need for vaccine technologies that can protect against these threats. DNA vaccines can be developed and manufactured rapidly compared with conventional vaccines, and so are prime candidates for vaccinating against these diseases. The early testing of Ebola vaccine compounds points toward this unmet need.

COMMERCIAL STATUS OF DNA VACCINE TECHNOLOGIES

First-generation vaccines (live attenuated microorganisms) include traditional, registered products. These vaccines are mature, with a long history of use. Second-generation vaccines (protein or protein components) are registered, and there is a continuing active search for new vaccines using these platforms. Many of these vaccine candidates are currently in clinical trials.

Third-generation vaccines (including DNA, viral/bacterial vectored, and autologous protein) are earliest in the technology life cycle, with important new technologies being discovered and tested in preclinical and clinical studies.

Thus, DNA vaccines can be considered an emerging vaccine platform, with a substantial number of vaccine candidates in early to mid-stage human clinical trials. There remains much late-stage clinical work to be done; however, this vaccine platform has shown sufficient promise in testing performed thus far to warrant serious attention by the vaccine industry.

The research tools segment is the most advanced commercially, with existing products in antibody generation (using genetic vaccination) and production of cGMP quality pDNA for preclinical and clinical studies. These markets are strategically significant for the DNA vaccine industry, as they provide tools for showing proof of concept of DNA vaccines in animal models and human clinical trials.

Several DNA vaccines for animal health have been introduced into the market, and there are additional vaccines under development for this market segment. DNA vaccines for animals have been easier to commercialize to date primarily because it is technically easier for a DNA vaccine to work in an animal than a

human, and the regulatory route to approval is easier for an animal than a human. As a result, the animal health market is at the leading edge of the DNA vaccine commercial efforts.

Human health applications, like cancer and infectious diseases, have the highest market potential, but are at an earlier stage in their commercial status. In order to commercialize human health DNA vaccines, substantial technical and regulatory hurdles must be surmounted. This requires significant commitment of time and resources by biotechnology and vaccine companies. Despite this, the biotechnology and vaccine commercial community is committing to this effort, as evidenced by the 96 current clinical trials and deep preclinical development programs. These efforts are supported by a critical mass of supporting industries, including DNA delivery, pDNA manufacturing, molecular adjuvants, and nanotechnology. These commercial factors are positive signs for eventual success in this market segment.

The structure for the traditional vaccine industry involved high barriers to entry (difficulty of manufacture combined with low market attractiveness). This limited the number of traditional vaccine manufacturers. Threat of substitutes is low in traditional vaccines because the technology is not changing rapidly. As a result, traditional vaccine manufacturers were able to establish an attractive vaccine franchise.

These structural forces within the traditional vaccine industry have resulted in a highly concentrated competitor situation with, for example, three producers (Sanofi Pasteur, Merck, and GlaxoSmithKline) supplying more than 70% of the US vaccine market.

The emergence of new (including DNA) vaccines is changing this traditional industry structure. Because the technology is new and rapidly evolving for these vaccines, substitute technologies and new entrants become a significant factor. Barriers to entry are lower than for traditional vaccines. As a result, emerging vaccine industries like DNA vaccines are more fragmented, with multiple product offerings targeted at a wide range of market segments.

At the same time, the vaccine industry is evolving much of the character of the pharmaceuticals business, with a focus on both prevention and treatment, infectious

diseases as well as cancer, and blockbuster market potential for any given product. The introduction of Gardasil (Merck), Cervarix (GSK), Rotarix (Merck), and Zostavax (Merck) followed the model of the first blockbuster vaccine, Prevnar (Merck). These vaccines, like the emerging DNA vaccines, target broad markets beyond the traditional limited pediatrician and specialist physician markets. DNA vaccines are expected to follow this new model, accessing substantial markets in infectious diseases, cancer, animal health, allergies, and biodefense.

This article is based on the following market analysis reports published by BCC Research: **Global Markets for Vaccine Technologies (PHM014E)** by Shalini Shahani Dewan and **DNA Vaccines: Technologies & Global Markets (BIO067B)** by Jon Evans For more information, visit www.bccresearch.com.

To view this issue and all back issues online, please visit www.drug-dev.com.

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