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PROFILE

Matrivax profile

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How and when did your company start, and where are you located?

Matrivax is a privately held, clinical stage biotechnology company developing human vaccines and immunotherapeutics for the prevention and treatment of life-threatening bacterial diseases. We were incorporated in October 2007 and are located in the major biotechnology hub of Boston, Massachusetts. Our company was established to develop a novel vaccine delivery platform technology discovered at Harvard University. We have advanced a vaccine candidate using this platform technology through a successful Phase 1 clinical trial.

How many employees do you have, and how do you find and attract them?

Matrivax currently employs 29 people, including 26 laboratory scientists. Many of our employees previously worked in the Boston area or graduated from local universities. We are fortunate to be in a world-class, highly innovative biotechnology community surrounded by some of the most prestigious academic institutions in the world. Prospective employees are attracted to our collegial, team-oriented work environment, commitment to employee career development, and passion for bringing novel vaccines and therapeutics to the clinic and advancing towards commercial development. Furthermore, we have relationships with several leading New England universities from which we attract students for internships. Our internship program has been highly effective in recruitment of talent.

What are the main focus and platform technology(ies) of your company?

Protein Capsular Matrix Vaccine (PCMV) technology, exclusively licensed from Harvard University, is the principal vaccine delivery platform in development at Matrivax. PCMV technology is an alternative to the typical polysaccharide conjugate technology used in the manufacture of several commercially available vaccines against bacterial pathogens (e.g. Prevnar 13®, a pneumococcal vaccine; Hib, a *Haemophilus influenzae* vaccine; and Menveo®, a meningococcal vaccine). In a PCMV, the capsular polysaccharide antigens of bacteria are non-covalently entrapped in a matrix of crosslinked protein rather than being covalently linked to the protein, as done in the manufacture of a conjugate vaccine. The PCMV process has the potential to transform the complex and expensive manufacture of conjugate vaccines into a simpler, less expensive process that can provide vaccines against emerging and existing capsular serotypes of infectious bacteria to the developed and developing world.

Can you provide a short overview of your product pipeline?

Recently, Matrivax successfully completed a Phase 1 proof-of-concept clinical study with Typhax, a typhoid fever PCMV candidate in development. Typhax is composed of the Vi capsular polysaccharide isolated from *Salmonella typhi* entrapped in a crosslinked matrix of an immunogenic protein commonly used in the manufacture of conjugate vaccines. Results from a dose-escalation Phase 1 study in healthy human subjects demonstrated that Typhax was well-tolerated and immunogenic.

Matrivax is also developing PCMV candidates targeting *Streptococcus pneumoniae* and *Clostridium difficile* along with protective protein antigens from both bacteria that will be used in conjunction with PCMV candidates to provide added protection against disease. Pre-clinical proof-of-concept has been demonstrated for candidate vaccines for the prevention of pneumococcal disease and *C. difficile* infection. These prophylactic and therapeutic vaccine candidates are actively being developed and characterized for clinical evaluation.

Who is your competition, and what advantage(s) do your products / technology offer?

There are several vaccines—either commercially available or at various stages of clinical development—that target typhoid fever (Typhim Vi®, Sanofi; Typherix®, GSK), pneumococcal disease (Prevnar 13®, Pfizer; Pneumovax 23®, Merck, both licensed) and *C. difficile* infections (Sanofi and Pfizer each have a vaccine candidate in Phase 3 trials). PCMV technology has three major advantages over conjugation technology with respect to ease of manufacture. The biggest advantage is that multiple polysaccharide antigens can be entrapped in a single PCMV reaction whereas in a conjugate vaccine each polysaccharide is chemically linked to the protein carrier in a separate reaction. For a multivalent polysaccharide based pneumococcal vaccine, this is a huge advantage as the current licensed vaccine commercial vaccine

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currently contains 13 polysaccharide serotypes, a number that will likely increase in future pneumococcal polysaccharide conjugate vaccines as new serotypes emerge. Another advantage of PCMV technology is that it requires no derivatization or resizing of the polysaccharide antigen which reduces the number of manufacturing steps and maintains native immunogenic epitopes of the polysaccharide antigen. Lastly, since polysaccharide antigens in a PCMV candidate are non-covalently entrapped in a crosslinked protein matrix, the process is independent of the polysaccharide composition and structure and thus only requires a single crosslinking chemistry. This is often not true for multivalent conjugate vaccine in which the crosslinking chemistry needs to be tailored to each polysaccharide. Based on these advantages, we anticipate being able to develop multivalent PCMV candidates with significantly reduced cost-of-goods compared to a conjugate vaccine.

Furthermore, Matrivax is investigating other proprietary vaccine technologies which may provide enhanced immunogenicity in patient populations that typically have a less than optimal response to existing vaccines, including the elderly and immunocompromised patients.

What were the "highlights" in your recent product development?

The most notable highlight is that Matrivax recently demonstrated that Typhax is both safe and immunogenic in humans in a Phase 1 clinical trial providing proof-of-concept for the PCMV platform technology. The data from this trial are compelling and may provide a framework for reducing the scope and cost of regulatory approval.

In pre-clinical murine studies, we have demonstrated that immunization with monovalent and multivalent *S. pneumoniae* PCMV candidates can elicit anti-polysaccharide antibody titers equal to or greater than commercialized conjugate vaccines. Furthermore, we have demonstrated that addition of a proprietary antigen to a PCMV candidate demonstrated a synergistic effect which delayed onset of disease symptoms in an experimental murine model of pneumonia. In the *C. difficile* vaccine arena, Matrivax has demonstrated in two distinct preclinical animal models that a vaccine candidate containing both protein and polysaccharide antigens provided superior protection compared to each antigen separately. Development of scalable purification processes for protein and polysaccharide antigens is in progress and GMP production is scheduled to begin in 2018.

An important highlight was the recruitment of additional laboratory scientists to expedite the preclinical development of future PCMV vaccine candidates for clinical studies. In the past year alone, Matrivax has grown from 17 to 29 employees.

What have been the most critical problems in developing products in your field, and how can your company's technology help overcome these problems?

A growing concern for polysaccharide-based vaccines against *S. pneumoniae* is the emergence of serotypes that are not covered by existing efficacious, pneumococcal vaccines. New polysaccharide serotypes will need to be incorporated into the current vaccine to cover these emergent strains which in turn increases manufacturing costs. Since the cost of many conjugate vaccines are already too high for developing countries, technologies, like PCMV, that reduce manufacturing costs would allow increased global access to efficacious polysaccharide-based vaccines that cover existing and emerging serotypes. Matrivax is exploring the addition of a broadly protective proprietary antigen to our vaccine candidate which would provide serotype independent immunity and expand the protection of a polysaccharide based vaccine.

Current vaccine and immunotherapy approaches for the prevention and treatment of *C. difficile* infections are focused on toxin A and/or toxin B, the primary cause of disease symptoms. Our approach is to develop a vaccine that targets both extracellular toxins and the toxin-producing bacteria through their cell surface polysaccharides. This two-pronged approach seeks to neutralize the toxins and diminish, or potentially eliminate, the bacteria. This combined approach will improve on the existing toxin-directed interventions by increasing prevention, improving therapeutic treatment, and potentially preventing recurrence.

A significant headwind for development of any new vaccine is the scope and duration of the clinical program required to obtain regulatory approval. For both scientific and ethical reasons, elicited antibody titers often can be used as a basis for regulatory approval of a new vaccine when another licensed vaccine has been shown to prevent disease caused by the same bacterial pathogen. Matrivax will propose this approach with global regulatory authorities as a basis for approval of pertinent PCMV candidates.

What is your company's value proposition?

Matrivax is a clinical stage company with a diverse portfolio of vaccines and immunotherapies for the prevention and treatment of life-threatening infectious diseases. Our technologies have the potential to both shorten the time and reduce the costs of manufacturing polysaccharide based vaccines, increase protection against new and emerging serotypes, and broaden global access to lifesaving vaccines and therapies.

What business development strategy do you pursue?

Matrivax has established active collaborations with researchers at several universities around the world and actively seeks new collaborators with innovative vaccine technologies. Matrivax has successfully licensed multiple enabling technologies to incorporate into our product pipeline.

How does your company attract partners?

Matrivax is in active discussions with potential partners to in-license additional technology that represent a strategic fit for the company. Our most natural partnerships are formed with companies that share our passion for efficient and effective solutions to global public health challenges.

Who are your most important partners?

John J. Mekalanos, PhD, Professor at Harvard Medical School is the inventor of PCMV technology and a member of the Board of Directors for the Company.

Gerald Chan, PhD, co-founder of the Morningside group and a member of the Dean's Board of Advisors of the Harvard

School of Public Health, shares in our vision of developing novel solutions that can be manufactured at reduced cost to contribute to health care delivery, particularly for countries with limited resources.

Matrivax recently announced an agreement with Stellar Biotechnology and the University of Guelph in which Matrivax acquired exclusive proprietary rights to protective *C. difficile* antigen targets. Additional in-licensing discussions are ongoing and will be announced publicly in the near future.

How do you balance performing work in-house vs outsourcing?

Matrivax develops the antigen purification procedures, conducts initial process development, develops characterization and release assays, and conducts nonclinical immunogenicity and protection studies in-house. We use outside providers to conduct GMP manufacture of antigens and PCMV candidates, GLP animal toxicology studies, and clinical research studies.

What are your product development goals for the next 3 years?

1. To establish a partnership to co-develop and commercialize Typhax.
2. To complete two or more clinical trials with our pneumococcal and *C. difficile* vaccine candidates. For more information, please visit: http://www.matrivax.com