Pfizer Vaccine Research and Development

Vaccines are one of the greatest public health advances of all time, resulting in the control, elimination, or near-elimination of numerous infectious diseases that have plagued humankind since time immemorial, generating tremendous value by preventing disease and sustaining healthy communities. For every $1.00 the U.S. spends on childhood vaccinations, we save $10.20 in disease treatment costs.¹

Today, Pfizer is building on our world-leading Prevnar franchise, to expand the benefits of vaccines to more patients across ages and geographies. This includes tackling deadly adult and adolescent infectious diseases, and evaluating therapeutic vaccines for chronic disease and conditions.

Pfizer’s Vaccine R&D strategy is to:

1. Continue to lead in pneumococcal disease prevention
2. Advance vaccines for deadly infections in adults and adolescents
3. Harness the power of vaccines for therapeutic uses
4. Continue to innovate on vaccine technologies

From pre-clinical to post-marketing programs, our pipeline is rooted in innovative proprietary vaccine technologies – and designed to address some of the world’s most pressing health needs.

1) Pneumococcal Disease Prevention

Pfizer is committed to maintaining its leadership position in the prevention of pneumococcal disease, and is expanding the impact of Prevnar into new age groups and geographies.

- Pneumococcal disease
  - Pneumococcal disease can affect people at any age, but older adults, as well as infants, are particularly at risk.²
  - Pfizer is exploring the potential impact of Prevenar 13 in older adults via the Community-Acquired Pneumonia Immunization Trial in Adults (CAPiTA).
  - CAPiTA is the largest vaccine efficacy trial ever conducted. It is a double-blind, randomized, placebo-controlled efficacy study to assess vaccine-mediated prevention of community-acquired pneumonia (CAP).³ It involves approximately 85,000 subjects aged 65 years and older⁴ and is the first ever conducted with a
conjugated vaccine to evaluate CAP at this scale. CAPiTA was designed to evaluate whether Prevenar 13 (a conjugated pneumococcal polysaccharide vaccine) is effective in preventing CAP caused by the 13 pneumococcal serotypes included in the vaccine.4

- Case accrual was completed in August 2013. Once unblinding occurs, Pfizer, Julius Clinical, and the primary investigator will review the data and disclose the top-line results, which is expected to occur in early 2014.

2) Preventing Deadly Infections

Pfizer’s clinical-stage vaccine programs target some of the most deadly adult and adolescent infectious diseases including:

- **Meningococcal B**
  - The vast majority of meningococcal disease has historically been caused by one of five types of bacteria, called “serogroups”: A, B, C, Y and W-135.5,6,7
  - According to the World Health Organization, meningococcal B bacteria is a leading cause of endemic meningitis in industrialized countries, accounting for 30 percent to 40 percent of the cases in North America and up to 80 percent of cases in some parts of Europe.8
  - Adolescents and young adults—even healthy ones—are at risk for meningococcal disease. While the risk of transmission has been linked to differing factors, such as living in dormitories, smoking or contact with smokers, frequenting bars or nightclubs and intimate kissing, the exact cause is not fully understood.9,13,14,15,16
  - Pfizer’s meningococcal B vaccine candidate – currently being studied in a Phase 3 trial – has the potential to be the first vaccine available in the U.S. for the prevention of meningococcal B disease in adolescents and young adults, who are the primary carriers of the disease-causing bacteria.

- **Staphylococcus aureus infection**
  - *Staphylococcus aureus* is a serious issue in hospitals, long-term care facilities and the community at-large. There is currently no vaccine available to prevent this serious infection and sometimes deadly disease, which can manifest itself in a number of diverse ways.
    - There are an estimated 80,000 cases of severe MRSA every year, resulting in approximately 11,000 deaths.17
  - Pfizer’s vaccine candidate for *Staphylococcus aureus* contains four distinct antigens which elicit anti-bacterial antibodies that kill *Staphylococcus aureus* and neutralize important bacterial virulence factor.
  - We recently concluded a Phase 2a study which showed encouraging signals that the vaccine elicits positive immune response. We anticipate sharing results in 2014 at a key medical congress.
  - The next step is to move into a Phase 2b study in surgical patients.
  - Patients who contract *S. aureus* in the post-surgical setting have been shown to have increased mortality, longer length of hospitalization, and a greater cost of care.18
- **Clostridium difficile colitis**
  - *C. difficile* is a growing, hard-to-treat infection in the hospital and long-term care setting and there are currently no vaccines available to prevent the disease.
  - The Centers for Disease Control and Prevention estimates approximately 250,000 cases of *C. difficile* are reported each year, causing 14,000 deaths.\(^{19}\)
  - Pfizer’s vaccine candidate, currently in Phase 1 clinical trials, is designed to prevent *C. difficile*-associated disease (including severe life-threatening diarrhea, pseudomembranous colitis) that is caused by two bacterial associated toxins, A and B, particularly in adults in at-risk settings (e.g., residing in long-term healthcare facilities, or undergoing antibiotic therapy in a hospital setting).

3) **Vaccines for Therapeutic Uses**

At Pfizer, we are exploring whether vaccines can do more than prevent disease and have a number of therapeutic vaccines in clinical development that may be used as potential treatments for chronic conditions or diseases.

We believe therapeutic vaccines may have longer-lasting benefits compared to traditional medicines and are currently conducting clinical trials with vaccines targeted towards:

- **Smoking cessation**
  - According to the CDC, cigarette smoking is the number one risk factor for lung cancer and in the United States, causes about 90% of all lung cancers.\(^{20}\) People who smoke are 15 to 30 times more likely to get lung cancer or die from lung cancer than people who do not smoke.\(^{20}\)
  - Those looking to quit smoking are in need of a novel aid that can help them quit, but not relapse once treatment stops.
  - Pfizer’s novel vaccine candidate induces anti-nicotine antibodies that prevent nicotine from entering the central nervous system (brain), thus removing the “reward” component from smoking, making it easier for those addicted to nicotine to quit and not relapse.

- **Allergic rhinitis/asthma**
  - Nearly 1/3 of the US population (around 75 million Americans) has an allergy and/or asthma\(^{21,22}\), with at least 50% of asthma and rhinitis being allergic in nature.\(^{23}\) Control of asthma continues to be a problem in the U.S.\(^{24}\)
  - The incidence of asthma continues to grow in both the U.S. and worldwide currently estimated at 300 million people and projected to increase to 400 million by 2025.\(^{25}\)
  - Pfizer is exploring treating allergic diseases such as asthma and allergic rhinitis for patients who have moderate to very severe, poorly controlled disease, by targeting the key mediator of allergy, IgE, and stimulating the body to produce anti-IgE cross reacting antibodies that decrease IgE levels in patients. It is believed this may reduce and prevent allergic and asthmatic symptoms.
Pfizer believes that a therapeutic vaccine that lowers IgE has the potential for a convenient and sustained treatment of allergic disease, with the added benefit of infrequent dosing requirements.

- **Cancer Vaccine-Based Immunotherapy Candidate**
  - We are conducting pre-clinical studies of a cancer vaccine-based immunotherapy candidate that reflects our understanding of the active elicitation and importantly, the maintenance of anti-tumor immune responses.
  - The basic science for this vaccine-based immunotherapy entails an active immunotherapy approach as the immune system plays a significant role in controlling the development and destruction of cancerous cells in individuals.

4) **Innovate New Technologies**
Pfizer’s industry-leading scientists and researchers are leveraging advanced technologies to usher in a new era of vaccine innovation. These include:

- **Antigen presentation technology** – Pfizer is continuing to study novel conjugation and carrier systems in vaccine R&D that can support better immune response. Our work here was made possible largely through our expertise on Prevnar 13 and we are actively applying some of these learnings to a number of other programs.

- **Adjuvant technologies** – Adjuvants are added to vaccines to enhance their profile and sometimes increase the duration of effect.

- **Novel vaccine delivery** – Pfizer is exploring novel systems so that the next generation vaccines will provide added convenience for patients and doctors.

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21. Asthma and Allergy Foundation of America (AAFA). Allergy Facts and Figures. Available at http://www.aafa.org/display.cfm?id=9&sub=30#
23. Asthma and Allergy Foundation of America (AAFA). Allergic Asthma. Available at http://www.aafa.org/display.cfm?id=8&sub=16