

RSV Vaccine PEV4

Seasonal RSV epidemics affect the population similarly to influenza, however, in contrast to influenza there is practically no prevention available. Pevion Biotech is developing a state-of-the-art subunit vaccine based on a recombinant protein antigen that is formulated with Pevion Biotech's market-approved virosomes. The vaccine candidate achieved excellent results in preclinical studies and has a first-in class potential.

MEDICAL NEED

Respiratory syncytial virus (RSV) has a high prevalence in developed countries. Although RSV is traditionally regarded as a pediatric pathogen, RSV can also cause life-threatening lower respiratory tract illness (LRI) in the elderly and in immunosuppressed individuals. RSV disease affects the elderly and high-risk adults as much as influenza does. Approximately 5% of elderly people become infected with RSV in seasonal epidemics every year, leading to pneumonia in 10 to 55% of the patients.

Infants and toddlers are at risk as well. By the age of two years, almost all children have experienced an infection with RSV, and approximately 50% have been infected twice. There is currently no vaccine against RSV available, and there is no specific therapeutic treatment available for individuals with acute RSV disease. The only treatment is passive immunization with a monoclonal antibody (Palivizumab[®], Medimmune), which is licensed only for prophylaxis in infants and children at high risk of developing severe RSV disease. The development of an RSV vaccine thus offers a first-in-class opportunity.

RATIONALE FOR VACCINE DESIGN

Immunosenescence and concomitant medical conditions make the elderly particularly vulnerable. While healthy adults are generally protected against severe RSV infection and disease, diminishing immunity against RSV with increasing age renders the elderly susceptible again. They require a vaccine design capable of boosting a weak immune system while still fulfilling the increased safety demands. Pevion Biotech's virosome technology responds extremely well to the combined needs for an enhanced immune response and the use of the vaccine in vulnerable populations. The excellent track record of Pevion Biotech's virosome technology gives it a competitive edge over other approaches in the RSV field.

The F protein of RSV is widely recognized as the most promising target antigen. The surface F and G proteins are the only viral components that induce RSV neutralizing antibodies, with the F protein showing much less strain variation than the G protein. Moreover, the G protein has been associated with potentiation of disease. The efficacy of neutralizing antibodies against the F protein has been clinically validated through monoclonal antibody therapy (Palivizumab[®] [Synagis] and Motavizumab[®] [in FDA review]). The use of a whole protein requires the employment of a suited carrier to achieve stabilization and presentation it in its natural conformation. The right conformation is crucial to favor recognition by specific B cell receptors, leading to the production of antibodies which indeed have neutralizing activity. Such carrier capabilities are provided by Pevion Biotech's virosome technology. The goal is to elicit a strong neutralizing antibody response and to avoid any risk of enhanced disease. The F protein is produced in mammalian cells using recombinant technology, thereby avoiding elaborate virus production. Pevion Biotech has evidence that

Key advantages of Pevion Biotech's RSV vaccine

- Use of recombinant and stabilized, whole F protein as most promising target
- Demonstrated efficacy of carrier & adjuvant system for high-quality B cell responses to subunit antigens
- Market-approved safety of carrier & adjuvant system, especially in elderly people and infants
- Established GMP manufacturing of carrier & adjuvant system on a commercial scale

the use of recombinant, whole F protein is the key to a successful vaccine development.

VACCINE PROFILE

Pevion Biotech is developing a state-of-the-art RSV vaccine (PEV4) especially for elderly people >60 years of age, who have particular safety and efficacy requirements. In a later stage of development, application of the vaccine may be extended to infants, another critical subpopulation with similar needs. The vaccine candidate uses recombinant RSV-F protein, purified from mammalian cells and formulated with Pevion Biotech's virosomes. The vaccine is suited for combination with a seasonal or broadband influenza vaccine product.

EXCELLENT PRECLINICAL RESULTS

Results from preclinical studies with Pevion Biotech's RSV vaccine candidate PEV4 in both mice and cotton rats are very promising. Proof of concept was demonstrated *in vivo* and further validated by ex vivo analytics. In summary, key findings are as follows:

- PEV4 elicited anti-F protein antibody levels as high as found after infection with wild-type virus.
- PEV4 induced antibodies which recognize both the parental virus and the isolated authentic viral F protein, and neutralize the virus in a dose-dependent manner.
- Several independent challenge studies demonstrated that immunization with PEV4 resulted in a dose-dependent reduction of viral load in nose, throat and lung (see Figure).
- After challenge, no histopathological changes in lung tissue were observed in animals immunized with PEV4.

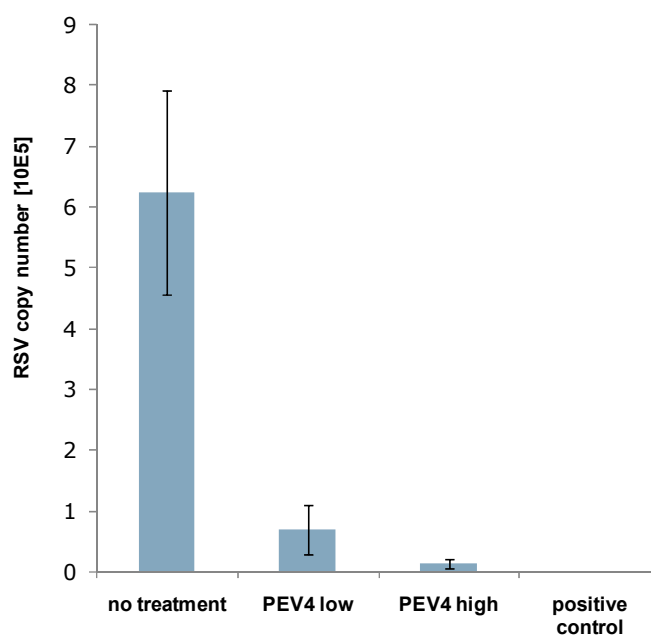


Figure: Challenge study in mice. Mice were immunized with the RSV vaccine (PEV4) and then challenged with RSV. Immunized mice showed a significant and dose-dependent reduction of viral load in the lung.

DEVELOPMENT STATUS

Preclinical efficacy studies of the vaccine have been completed and proof of concept in an animal model has been achieved. Process development for the manufacturing of the F protein is currently ongoing. GMP production I and toxicology studies are planned for 2010. Pevion Biotech expects to enter a first

clinical trial in 2011. The company plans to conduct a combined clinical Phase I/II study in healthy volunteers with a controlled virus challenge. The combined study design will allow rapid achievement of proof of concept in humans.

IP SITUATION

Pevion Biotech has a complete patent portfolio of virosomes which covers all aspects and applications of the virosome technology platform. With regard to the RSV-F protein, Pevion holds exclusive license rights to a codon-optimized DNA sequence for recombinant expression in mammalian cells. Pevion Biotech has freedom to operate for its RSV vaccine candidate.

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