

- **Novel multi-protein vaccine against pneumococcal disease, with strong preclinical and human phase 1 data, addressing significant unmet market needs:**
 - ✓ **Confers broad cross serotype responses**
 - ✓ **Cost effective**
- **Plan to license or co-develop progression into Phase 2 onwards**

Meeting Unmet Market Needs

Despite vaccines being available, invasive pneumococcal disease remains the leading source of death from any cause in the under 5 year old age group globally. This results on average in a death every 15 seconds. Pneumococcal disease is also a major source of morbidity in the elderly.

The current vaccine products, despite limitations, are already widely used and many countries include a vaccine against *Streptococcus pneumoniae* in their standard schedule. However, the protection conferred by existing products is restricted to a sub set of serotypes. Unfortunately, alternative serotypes are now beginning to replace the strains targeted by existing products. Critically, the production costs for existing vaccines are inherently high. A broadly-protective and cost-effective vaccine would be used universally.

The emergence of new pathogenic strains and of antibiotic resistance increases the need for new prophylactic vaccines with a broad protective capability.

Market

The market value is dominated by the leading vaccine, Pfizer's Prevnar, achieving over \$6B in revenue in 2015. PnuBioVax, ImmBio's solution, has the potential for wide market impact, reducing the overall cost of the vaccination schedules and facilitating entry into new markets, with a broadly protective product.

Product Design

For *S. pneumoniae*, strain variation of the polysaccharide component is substantial. Polysaccharide Conjugate Vaccines (PCVs) such as Prevnar generate good killing activity for the strains incorporated in these multivalent vaccines. In contrast, the protein composition of *S. pneumoniae* is less variable especially for specific proteins such as pneumolysin (Ply) that does not come under strong selective pressure.

PnuBioVax™ is based on ImmBio's innovative ImmBioVax technology platform. The vaccine contains a range of proteins including Heat shock proteins and proteins complexed with Hsps (HspC). Hsp both directly stimulate the innate immune system and effectively deliver protein cargo to dendritic cells to greatly facilitate antigen presentation. This delivers vaccine efficacy without the need for the addition of adjuvants reducing cost and potential safety concerns. The wide array of antigens presented successfully provides broad protection to distinct populations and ages.

The target is a lyophilised vaccine.

Development Status

Following positive data from other ImmBioVax vaccines, ImmBio initiated the project against *S. pneumoniae* in collaboration with the University of Bristol, University College London and the Institute of Child Health, UCL. A Scientific Advisory Group of key opinion leaders supports the PnuBioVax development strategy.

Process development has built on experience with other ImmBioVax vaccines. Extensive pre-clinical studies now show that:

PnuBioVax induced antibodies

- Bind to multiple pneumococcal protein targets (Western, MSD) with evidence of cross-reactivity
- Bind to live pneumococci across serotypes
- Specific targets include Ply and PspA
- Anti-Ply antibodies are functional (neutralising) across serotypes
- Opsonophagocytic killing of some serotypes, including those not covered by Prevnar
- Passive transfer to mice provides protection against homologous and heterologous challenge

PnuBioVax induces a specific T-cell response

- Measured by IL-17 stimulation by pneumococci in mouse splenocytes and by vaccine in human PBMCs

PnuBioVax preclinical data support multiple Mechanisms of Action, notably prevention of carriage, with IL-17 as a key marker, killing activity and neutralisation of Ply, a key source of tissue damage and disease progression. Data extend beyond the strain panel typically covered by the PCVs. Further studies on the Mechanism of Action are ongoing at the Murdoch Institute, Australia

Manufacturing Process

ImmBio has established a genetically modified master cell bank that expresses detoxified Ply. After fermentation and stress induction, the downstream process is centred on ion exchange chromatography. Assays and characterisation studies have been central in establishing a stable, high-yielding, reproducible process within a defined specification.

Product consistency data include batch-to-batch and scaling runs using assay methods discussed with Regulatory Agencies in Germany (PEI)

and the UK (MHRA). The process runs at 10 L scale at a CMO in Australia to cGMP, with a yield > 4,000 clinical doses/10 L.

Human Phase 1 Study

Following MHRA approval, PnuBioVax has successfully completed First in Man clinical study. It is a placebo controlled double blind study, at three dose levels, each a prime and two boosts, in male and female adults. The primary endpoint were safety and selected immunogenicity against placebo and pre-vaccination baseline. Secondary endpoints were range of immunological markers to investigate the potential impact on carriage, T cell and antibody generation, including neutralisation of pneumolyin.

PnuBioVax has been found in human study to be well tolerated and immunogenic.

Robust Proprietary Position

PnuBioVax™ is based on ImmBioVax technology. ImmBio owns a broad, strong IP estate, with families of patents covering composition, mode of action and process.

Key Competitive Advantages

- Unique ability to deliver broad protection
- Safety profile expected to be excellent.
- Cost effective, approvable manufacturing process.

The partnering opportunity

ImmBio is interested in expressions of interest for co-development and clinical trial partnership. This may be at either a regional or global level.

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