Overview of Allergy Therapeutics

- Fully integrated biopharmaceutical company specialised in immunotherapy to treat allergies
  - A leading provider of subcutaneous aluminium-free allergy vaccines in our markets in Europe
  - Gross sales CAGR of 9% since 1999
- Key products include Pollinex Quattro® (49% of Group revenue), a proprietary formulation technology platform
  - Enables an effective, ultra-short course treatment
- Sales and marketing network comprising c.118 pan-European sales force and various distribution agreements
- European market share increased from 8.7% to 10.1% over last 2 years
- Strong new product pipeline
- Poised to execute a pivotal clinical trial programme to enable access to US – estimated $2bn market size
- Headquartered in Worthing, West Sussex, c.420 employees
Immunotherapy: Leading AR market growth

- Immunotherapy, the only disease modifying Allergic Rhinitis (AR) therapy, is expected to grow at a CAGR of 11% to 2020*, compared with a CAGR of 3% in the total AR market.
- Immunotherapy market share forecast to increase from 10% to 18% by 2020, becoming a US$2.5bn market.
- The main growth driver is the potential US$2bn US market which is currently unregulated for subcutaneous immunotherapy treatment.

*Source: Visiongain, AR forecast 2014
Sales breakdown based on gross sales at budget exchange rates (before freight, discounts, rebates and exchange) : £49.3 million.
After deducting discounts, rebates, freight charges and foreign exchange adjustments, total sales for FY2015 is £43.2 million.
Global presence

Subsidiaries in 9 countries and distribution agreements in additional 10 countries

1) Sales breakdown based on net vaccine sales (after discounts) plus licences: £44.2 million.
After deducting rebates, freight charges and foreign adjustments, total sales for FY2014 is £42.0 million.
Pollinex Quattro is a platform technology that combines modified allergens (known as allergoids) and MCT* (a natural depot adjuvant) in a mixture containing the adjuvant MPL*, an immune system booster.

- Allergy Therapeutics has rights to MPL from GSK for allergy vaccines.
- Subcutaneous aluminium free immunotherapy principally for grass, tree and ragweed allergies.
- Ultra-short course: 4 injections in 3 weeks, efficacy in 3 weeks.

*See Slide 31 for further details.
Allergoid
• Allergen chemically modified with glutaraldehyde
• Reduces IgE reactivity vs. that induced by native allergens used in SIT
• Retains IgG-allergen stimulating properties

MPL Adjuvant
• MPL (Monophosphoryl Lipid A) is a non-toxic derivative of lipopolysaccharide (LPS)
• Acts locally as a TLR4 agonist and increases IgG production
• Regulates expression of co-stimulatory molecules on antigen-presenting cells
• MPL allows the SIT treatment course to be shortened (big impact on adherence)

Micro Crystalline Tyrosine (MCT)
• A natural amino acid which is readily metabolized
• L-tyrosine retains the Allergoid and MPL at the site of injection (half life = 48 hours) as depot
• 30-year history of safe use in vaccines
• Rebalances TH1 response
Growth strategy

1. **Organic Growth Strategy**
2. **Inorganic Growth Strategy**
3. **Biotech: Launch in the US**

1 + 1 = 3
Organic growth: Current trading and future opportunities

- Trading for first four months of FY16
  1. Strong trading in first four months of current financial year as we continue to grow market share
  2. Revenue Growth of 15% on a constant currency basis (12% excl. Alerpharma acquisition)
  3. Strong growth in Europe across Germany, Austria, Netherlands, Spain & Italy

- Organic new projects leveraging current infrastructure
  - **House Dust Mite**: Acarovac Plus → Acarovac Quattro
    - Internally developed
    - Pollinex Quattro Technology Applied to the Perennial Market
    - Est. market size $3-4bn (worldwide)
    - Competitive environment: marketed long-course products
  - **Immunomodulators and adjuvants**
    - Symbiotics: immunomodulators for allergy response
    - MCT adjuvant systems: to be used with other vaccines
1. Alerpharma acquisition – successful on-going integration
   - Spain is our second most important allergic rhinitis market but we had the lowest market share
   - Merger with Spanish subsidiary provides
     - cross-selling opportunities
     - cost synergies
     - Increase product range
   - Outstanding manufacturing facilities
   - Accretive to the Group

2. Other small accretive opportunities exist
   - Allergy-related areas: products, companies or licensing agreements
   - Areas of focus: immunomodulators, diagnosis, dermatology, respiratory
   - Rigorous disciplines to maximise shareholder value
US Market:
The Opportunity
The US opportunity

- In the United States, over 80 million people suffer from Allergic Rhinitis*:
  - Diagnosis rates remain low at around 31%*

- Piper Jaffray Investment Research estimated U.S. allergy immunotherapy spending (including administration) at approximately $2 billion in 2008

- The US market, like Germany, is predominantly SCIT focused, but no current registered SCIT products

- Opportunity to register lead product, Pollinex Quattro Grass, in the US and be the first regulated SCIT seasonal mover into a potential US$2bn market ***

- Opportunity Fully Funded

- Clinical Development Plan on track. Estimated Launch: 2019

Source:  
*Datamonitor “Epidemiology: Allergic Rhinitis, March 2011
**The Current State of Therapy for Allergic Rhinitis in the United States. Lawrence DuBuske, MD.
***Piper Jaffray Update on the AR market, Sept. 2008
Impact of AR in the United States: a big unmet need

• Based on average impairment and prevalence estimates, allergic disorders ranked as fifth most costly chronic disease in the United States

• Allergic rhinitis estimated to cause:
  • 100 million days of lost work
  • 28 million days of lost productivity
  • 16.7 million physician office visits
  • 1.5 million missed school days
  • $5.9 billion in direct expenditure on treatment each year

• Allergen SIT practitioners in the United States currently use a wide variety of formulations, prepared for individual patients ad hoc from commercial source allergen extract solutions.

Source:
Immunotherapy: Main global players

- Four listed companies compete to lead the market in Europe and the US

- Products:
  - ALK:
    - Grastek: SLIT-Pill for grass allergy. Launched in the US
    - Ragwitek: SLIT-Pill for ragweed allergy. Launched in the US
  - Stallergenes:
    - Oralair: SLIT-Pill for grass allergy. Launched in the US
  - Allergy Therapeutics:
    - Pollinex Quattro: ultra-short SCIT for grass allergy. Not launched in the US
  - Circassia:
    - Toleroimmune: ultra-short SCIT for cat allergy. Not launched
Entry opportunity to the US

**Current US SCIT market**

- Long courses of treatment:
  - 50 to 100 injections
- Slow to act: 6 to 12 months
- Home made preparation:
  - Physicians mix the allergens
  - Non registered
- Non GMP manufacturing
- No clinical evidence
- Low compliance

**Allergy Therapeutics’ entry in the US**

- Ultra-course treatment:
  - 4 injections
- Efficacy in 3 weeks
- Standardised dose vaccine
- BLA to be submitted to the FDA in 2018
- GMP manufactured
- Multiple clinical studies showing efficacy and safety
- High compliance
US opportunity for Pollinex Quattro

1. Proprietary Technology
   - Pollinex Quattro’s platform technology:
     - ultrashort course in the market (4 injections p.a.)
     - aluminium free immunotherapy
     - only SIT product with an FDA approved adjuvant.
   - IP Protected

2. First Movers
   - First to market in the SCIT segment
   - High entry barriers: regulatory requirements for extensive trials on efficacy and safety

3. Strategic Fit for US market*
   - Pollinex Quattro is a SCIT product for a SCIT Market
   - Injectable vaccine therapy expected to be accepted by allergy specialists who are familiar with SCIT products

4. De-risked opportunity
   - Pollinex Quattro has already treated more than 200,000 patients and been marketed in 7 countries
   - Building on Progress to date in the US:
     - US$100 million invested in clinical studies to date
     - 14 clinical trials completed to date, including Phase I, II & III successful studies
     - Investigated in over 3,000 patients worldwide, mainly in the US

Source: *The Current States of Therapy for Allergic Rhinitis in the United States. Lawrence Du Buske, MD.
US opportunity for Pollinex Quattro

- The main pollen allergens, Grass, Trees & Ragweed, have a prevalence on the population of approx. 50%, 30% and 26% respectively*

- We estimate Pollinex Quattro Grass could reach peak sales of around 30% of the potential market in 4-5 years from US launch:
  - Under our assumptions, PQ Grass would reach annual sales of between US$300 million and US$400 million in that period
  - Total Pollinex Quattro vaccines, including Trees and Ragweed, could potentially lead to annual sales of between US$ 700-800 million 4-5 years from final launch in the US market

Peanut Allergy:
The Opportunity
Commercial Opportunity

- Allergy Therapeutics has signed an agreement with Saiba GmbH acquiring exclusive rights to develop VLP based allergy vaccines in humans.
- First development will be a VLP based immunotherapy for peanut allergy - the most common cause of anaphylaxis and death due to food-allergic reactions.
- The World Allergy Organization estimates that up to 520 million people may have food allergy.
- Additionally, the prevalence of food allergy is increasing according to the Centres for Disease Control and prevention:
  - Food allergy in children increased from 3.4% between 1997 and 1999 to 5.1% in 2009 to 2011.
  - That’s an increase of 50% in a decade!
Peanut vaccine: Unmet need

- The market for food allergy therapies is a multi-billion dollar opportunity*

- An estimated 5.1% of children in the US had a food allergy in 2009 to 2011 (Centre for disease control)

- According to the Centres for Disease control an prevention that figure represents an astounding 50% increase in prevalence from the late 1990s

- Adverse reaction results in 200,000 emergency room visits in the US yearly

- Significant burden of disease (anaphylaxis!) caused by peanut allergy

- Peanut allergen avoidance challenging

* Piper Jaffray analyst note
VLPs are supra-molecular structures typically in the form of icosahedrons with diameters in the range of 20-100 nm.

They spontaneously assemble to particles looking like viruses. Importantly they incorporate the key immunological features of viruses which are responsible for the induction of fulminant immune response. These include repetitive surfaces, particulate structure, induction of innate immunity through activation of pathogen associated molecular patterns and T helper cell epitopes.

Recombinant expressed VLPs, while structurally similar to viruses, lack genetic information with replicative capacity and hence do not have the safety issues associated with whole virus vaccines.
Key highlights

1. Lead product Pollinex Quattro, a proven, unique and highly differentiated allergy vaccination

2. Integrated, efficient and scalable platform technology

3. Strong pipeline of aluminium-free allergy vaccines

4. Well established European commercial presence through direct sales force & distributors

5. MHRA-approved manufacturing facility with significant headroom

6. Strong financial performance with trend over 16 years of gross sales growth

7. Focused on the US opportunity & strengthening position in European allergy rhinitis market
Appendix
## Key marketed products

<table>
<thead>
<tr>
<th>Key marketed products</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>PROBIOTICS</strong></td>
<td>Dietary supplement based on symbiotic micro-encapsulated probiotics, Immunomodulators, Sold in Italy and Spain</td>
</tr>
<tr>
<td><strong>POLLINEX</strong></td>
<td>Licensed subcutaneous immunotherapy for grass and tree allergy containing MPL, The only immunotherapy containing 13 grass species, Sold mainly in Germany, UK, The Netherlands, Czech Republic and Slovakia</td>
</tr>
<tr>
<td><strong>POLLINEX QUATTRO</strong></td>
<td>Subcutaneous immunotherapy for grass and/or tree allergy containing MPL, Ultra short course; only 4 injections per year, Sold mainly in Germany, Austria, Italy and Spain</td>
</tr>
<tr>
<td><strong>ORALVAC</strong></td>
<td>Sublingual immunotherapy for grass, tree, HDM, cat, dog and moulds, Available in 517 variants, Sold mainly in Germany, Austria, UK, Italy and Spain</td>
</tr>
</tbody>
</table>
SLIT vs. SCIT: % SLIT evolution in Germany

- SLIT market has always been below 25%
- During last three years % is below 20% even with the launch Tablets

Source: IMS
### Completed clinical studies

<table>
<thead>
<tr>
<th>Programme/Study</th>
<th>Purpose</th>
<th>Location</th>
<th>Subjects</th>
<th>Status</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Grass</strong></td>
<td></td>
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<tr>
<td>Study 101</td>
<td>Residual allergenicity</td>
<td>US</td>
<td>12</td>
<td>Complete</td>
<td>2005</td>
</tr>
<tr>
<td>Study 201</td>
<td>Assay validation</td>
<td>US</td>
<td>70</td>
<td>Complete</td>
<td>2005</td>
</tr>
<tr>
<td>Study 202</td>
<td>Effects of MPL</td>
<td>Canada</td>
<td>40</td>
<td>Complete</td>
<td>2005</td>
</tr>
<tr>
<td>Study 203</td>
<td>Dose ranging</td>
<td>Canada</td>
<td>74</td>
<td>Complete</td>
<td>2005</td>
</tr>
<tr>
<td>Study 301</td>
<td>Phase 3 efficacy safety</td>
<td>N America and Europe</td>
<td>1,028</td>
<td>Complete</td>
<td>2007</td>
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<tr>
<td><strong>Ragweed</strong></td>
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<td></td>
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<tr>
<td>Study 101</td>
<td>Residual allergenicity</td>
<td>Canada</td>
<td>12</td>
<td>Complete</td>
<td>2005</td>
</tr>
<tr>
<td>Study 203</td>
<td>Dose ranging</td>
<td>US</td>
<td>68</td>
<td>Complete</td>
<td>2006</td>
</tr>
<tr>
<td>Study 204</td>
<td>EEC efficacy ± MPL</td>
<td>Canada</td>
<td>228</td>
<td>Complete</td>
<td>2006</td>
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<td>1 year f/u EEC efficacy</td>
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<tr>
<td>Study 301</td>
<td>Phase 3 efficacy &amp; safety</td>
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<td>993</td>
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<td><strong>Tree</strong></td>
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<td>Study 101</td>
<td>Residual allergenicity</td>
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<td>Canada</td>
<td>300</td>
<td>Clinical</td>
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</tbody>
</table>

Phase I, II and III studies were conducted across 3 INDs for the Grass, Ragweed and Tree MATA MPL products in the US, Canada and Europe, comprising ~3000 patients. The programme was placed on clinical hold by the FDA in 2007 which was lifted in 2012 and are available for BLAs. The first to be developed with be Grass MATA MPL for which we have received significant support and advice to the “path” to BLA (see Data Base Section 02.03.04.01.103).
2 years before launch of Pollinex Quattro Grass, we will analyse the best strategy to register and launch Pollinex Quattro Ragweed and Trees