The Future of Allergy Treatment
Ultra-Fast Allergy Immunotherapy
Anergis Focus on Allergy Immunotherapy (AIT)

- High Medical Need and Patient Demand
  - 500 M allergic patients - fastest growing chronic condition in industrialized world
  - Allergic rhinitis market (symptomatic and AIT) expected to grow to $15 bn by 2024
  - Marketed AIT (aka “desensitization”, “allergy shots”) requires 3-5 years of treatment

- Next Generation Allergy Treatment: Ultra-fast AIT
  - Proof-of concept established with lead product (birch pollen allergy, Phase IIb)
  - Proprietary platform technology based on long peptides applicable to most allergies
  - Preclinical pipeline of candidates
  - Market potential estimates from $0.5 bn to $1.5 bn per year and per product

- Privately held; raised $52 M private equity to date
Management Team

Vincent Charlon, PhD
Chief Executive Officer
25+ years global management and clinical development
• LS Pharma, Hesperion/Actelion
• Hoffmann-La Roche

Alexander Kettner, PhD
Head of Research
15+ years biology, peptides, immunology, patents
• University of Rome, Dept experimental medicine
• Harvard Medical School, Dept Immunology
• ETH Zurich, Biology

Vanya Beltrami, Pharm D
VP Head of Manufacturing
25+ years production and registration of injectables
• Merck-Serono
• Laboratoires Serono

Gerard Farmer, PhD, Regulatory
25+ years biotech, pharma regulatory and CMC expertise
• Alfomec Regulatory Consulting, Managing Director
• Ares-Serono, Corporate VP Regulatory Affairs

François Spertini, MD, Allergist
Founder
25+ years allergy medical practice
• Assoc. Prof. and Chief Allergy/Immunology
• Lausanne University Hospital (CHUV)

Pierre Morgon, PharmD, MBA
Marketing
25+ years pharma marketing
• Sanofi-Pasteur, Schering-Plough
• Bristol-Myers-Squibb

Name in italics = regular consultant

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Allergy is an Abnormal Immune Response

Exposure to **allergens**
bee stings, pollens,
house dust mites, pets, food

25-30% of the population

**Allergic immune response**
allergen linking **IgE antibodies**
release of inflammatory chemicals

**Allergy symptoms**
rhinitis, asthma, skin reactions
anaphylaxis

**Immunotherapy (AIT)**

Symptomatic treatment
(e.g. anti-histamine)

IgE: Immunoglobulin type E
The Allergic Rhinitis Market is Expected to Grow, Particularly Immunotherapy

2013: $11,056 m

2024: $15,207 m

3-Year Allergy Immunotherapy

10.6 %  
8% CAGR  
18.2%
Compliance to 3-Year AIT is Very Poor

Real-life compliance and persistence among users of subcutaneous and sublingual allergen immunotherapy

Menno A. Kiel, MD, MSc, Esther Röder, MD, PhD, Roy Gerth van Wijk, MD, PhD, Maiwenn J. Al, PhD, Nim C. J. Hop, PhD, and Maureen P. M. H. Rutten-van Molken, PhD

Rotterdam, The Netherlands

Subcutaneous AIT (SCIT) N=2796

Sublingual AIT (SLIT) N=3690

(J Allergy Clin Immunol 2013;132:353-60.)
## Ultra-Fast Allergy Immunotherapy

### 2 months instead of 3 years of treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>1\textsuperscript{st} year</th>
<th>2\textsuperscript{nd} year</th>
<th>3\textsuperscript{rd} year</th>
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<td><img src="image" alt="50 injections" /></td>
<td><img src="image" alt="Up to 1000 doses" /></td>
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COP: Contiguous Overlapping Peptides ; AIT: Allergy Immunotherapy
The Future of Allergy Treatment

Source: Business Insights May 2011, Anergis external market research and sales forecasts
COP Breakthrough Technology
A proprietary technology platform for ultra-fast allergy immunotherapy with contiguous overlapping peptides (COP)

<table>
<thead>
<tr>
<th>Natural Allergen Amino Acid Sequence</th>
<th>Long Contiguous Overlapping Peptides for Ultra-Fast AIT</th>
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<tr>
<td></td>
<td>COP-1  ABC---HIJK</td>
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<td>COP-2  IJL---PQRST</td>
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<tr>
<td></td>
<td>COP-3  QRSTU---XYZ</td>
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- Long peptides – all linear epitopes: ✔️ Efficacy
- Disrupted 3D structure: ✔️ Safety
- Synthetic GMP peptides: ✔️ Quality
- Safe at high doses: ✔️ Convenience

- Immunogenicity: No IgE binding
- Quality: Not like extracts
- Convenience: Ultra-fast treatment

AIT: Allergy immunotherapy; COP: Contiguous Overlapping Peptides; A-Z: amino acid; IgE: Immunoglobulin type E; 3D: three dimensional; GMP: Good Manufacturing Practice
Ultra-Fast AIT with COPs

COPs

Natural Allergen Amino Acid Sequence

Long Contiguous Overlapping Peptides for Ultra-Fast AIT

COP-1 ABC---HIJK
COP-2 IJKL---PQRST
COP-3 QRSTU---XYZ

Multiplication of activated dendritic cells

Enhanced proliferation

Accelerated tolerance/Anergy

APC: Antigen Presenting Cell; T reg: T regulatory cell
## Product Pipeline

<table>
<thead>
<tr>
<th></th>
<th>Discovery</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
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<tbody>
<tr>
<td>Birch</td>
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<td>COP selection</td>
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<td>Phase I/Ila</td>
<td>Phase IIb</td>
<td>Phase III</td>
<td>Market</td>
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COP: Contiguous Overlapping Peptides; alhydrogel: aluminum hydroxide
Birch Pollen Allergy

- Highly prevalent early spring tree pollen allergy (March - April)
  - Well described major allergen Bet v 1

- 50 million patients affected in North America and Europe
  - 50% have moderate to severe symptoms

- Global market research
  (290 prescribers, 870 patient records, 100 patients)
  - strong opportunity to improve patient acceptance and compliance, while decreasing overall treatment cost to society
  - annual peak sales potential $600 - $800 M (50% US/Canada, 50% Europe)
COPs: Undetectable Binding to Patient IgE
decreased more than $10^6$ fold compared to the allergen

**ELISA IgE competition assay**

- **Bet v 1 COPs**
- **Non binding control (BSA)**
- **Suboptimal peptides** (similar to allergoids)
- **Allergen (Bet v 1) or birch extract**

ELISA: Enzyme-Linked ImmunoSorbent Assay; BSA: Bovine Serum Albumin

COPs Do not Induce Anaphylaxis unlike the allergen, in the mice sensitization and challenge model

Mice were sensitized to rBet v 1 by injecting 0.1 μg rBet v 1 adsorbed to 2 mg aluminum hydroxide. rBet v 1-specific IgE (A), IgG1 (B) and IgG2 (C) were measured in mice serum harvested just before the next injection. Results were expressed as means±SD. C. Rectal temperature was recorded at indicated time points following 30 μg rBet v 1 (■) or 150 μg AllerT (◊) i.p. challenge at day 84 of the immunization protocol.

Clinical Development Experience
615 patients treated with AllerT SC 5-100 µg / injection

(AllerT SC = Bet v 1 COPs + alhydrogel in 5 subcutaneous injections)

- Phase I/IIa with immunology follow-up until Year 4
  - AllerT SC N=15 ; Placebo N=5

- Field-Based Year 1 Phase IIb + Year 2 Field Second Season
  - AllerT SC N=160 ; Placebo N=79

- Environmental Exposure Chamber Exploratory Dose Ranging
  - AllerT SC N=160 ; Placebo N=53

- Field-Based Year 1 ATIBAR trial
  - AllerT SC N=280 ; Placebo N=140
Safety and Immunogenicity
Clinical Phase I/IIa

- Double-blind, randomized AllerT (N=15) vs placebo (N=5)

- Allergen-dose equivalent to 3 years of allergy shots (450 µg total)
  - Day 1: 50 µg
  - Day 7, 14, 21, 51: 100 µg

- Safe and well tolerated

- Strong immunogenicity

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**Strong Immune Responses**
4 weeks after the last preseasonal injection

- Placebo
- AllerT

**Pellaton et al. Clinical and Translational Allergy 2013, 3:17**
Field Efficacy at Year 1 and Year 2
Clinical Phase IIb and follow-up

Sustained Clinical Efficacy over two seasons
without repeating treatment the second year

RSMS during second birch pollen season
Year 2 (Median RSMS, PP set)

RSMS: combined Rhinoconjunctivitis Symptom and Medication Score; MiniRQLQ: Mini Rhinoconjunctivitis Quality of Life Questionnaire; PP: Per Protocol

Spertini et al. JACI 2016
Kettner et al. JACI 2018
Immune Memory at Year 2 and at Year 4
Clinical Phase I/IIa follow-up

Allergen-Specific IgG4 after 2\textsuperscript{nd} and 4\textsuperscript{th} Season

Data (median) from blood samples collected in July 2012 from subjects allergic to birch pollen who had received 5 SC injections over 2 months of placebo or AllerT. All within group changes from baseline for placebo are NS. Placebo N=5, AllerT N=15.
Next Generation COP Allergy Vaccines

- The concept of Anergis’ ultra-fast AIT with COPs has been proven
  - Persistence of seasonal field efficacy over two consecutive seasons
  - Long lasting immune memory up to four seasons after a single treatment course

- The benefit-risk ratio of COP Allergy Vaccines needs improvement
  - ATIBAR trial < 20% efficacy vs placebo (CSMS -7%, p=0.0047)
  - Sensitization to the COPs in presence of aluminium

- The next generation of COP Allergy Vaccines without aluminum is in development with novel proprietary formulations

  → Enhanced efficacy: boosted immunogenicity with a dominant TH1 response

  → Improved tolerability: use of lower doses and no sensitization to the COPs
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Contact: info@anergis.ch