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 $15bn 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
Experienced Management Team

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

Kim Simonsen, MD
Chief Development Officer
25+ years clinical and biotech development
- Ablynx, ALK-Abello
- Medicin, Novartis, Novo Nordisk

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)

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

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

Name in italics = regular consultant

Company Milestones
2001 Foundation by F Spertini
2005 Acquisition of IP from University of Lausanne / EPFL / CHUV
2008 Start Clinical Phase I (2 trials)
2012 Start Clinical Phase II (3 trials)
2016 Start ATIBAR registration trial
2017 Results ATIBAR trial
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

**Symptomatic treatment**
(e.g. anti-histamine)

**Allergen Immunotherapy (AIT)**

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

Rotterdam, The Netherlands

Subcutaneous AIT (SCIT) N=2796

Sublingual AIT (SLIT) N=3690

(J Allergy Clin Immunol 2013;132:353-60.)
Anergis develops the Next Generation Ultra-Fast Allergy Immunotherapy

2 months instead of 3 years of treatment

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<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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COP: Contiguous Overlapping Peptides ; AIT: Allergy Immunotherapy
The Future of Allergy Treatment

- 2017
- 3-year AIT
- Ultra-fast AIT
  - $2-4 billion/year

Long-Lasting Allergy Symptom Relief after a Single Two-Month Treatment Course

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

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

Long peptides – all linear epitopes  ✓ Efficacy
Disrupted 3D structure  ✓ Safety
Synthetic GMP peptides  ✓ Quality
Safe at high doses  ✓ Convenience

Immunogenicity
No IgE binding
Not like extracts
Ultra-fast treatment

AIT: Allergy immunotherapy ; COP: Contiguous Overlapping Peptides ; A-Z: amino acid ; IP: Intellectual Property ; IgE: Immunoglobulin type E ; 3D: three dimensional ; GMP: Good Manufacturing Practice
Ultra-Fast AIT with AllerT (COP long peptides)

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

Enhanced proliferation

Accelerated tolerance/ Anergy

Multiplication of activated dendritic cells
## Product Pipeline

<table>
<thead>
<tr>
<th></th>
<th>Preclinical</th>
<th>Pre-IND</th>
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<th>Phase II</th>
<th>Phase III</th>
<th>Market</th>
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IND: Investigational New Drug ; Contiguous Overlapping Peptides
Lead-Product: AllerT (Birch pollen allergy)

- Highly prevalent early spring tree pollen allergy (Mar-Apr)
  - 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 2015
  (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 MM (50% US/CND, 50% Europe)
COPs: Undetectable Binding to Patient IgE
decreased more than $10^6$ fold compared to the allergen

**ELISA IgE competition assay**

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

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 of 0.1μg rBet v 1 adsorbed to 2mg Alum. 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 30μg rBet v 1(■) or 150μg AllerT (◊) i.p. challenge at day 84 of the immunization protocol.

Clinical Development Experience
335 patients treated with AllerT SC in completed trials

- Phase I skin prick tests safety study (AN002)
- Phase I/IIa with immunology follow-up until Year 4 (AN003)
  - AllerT SC N=15 ; Placebo N=5
- Field-Based Year 1 Phase IIb (AN004T)
  - AllerT SC N=160 ; Placebo N=79
- Field-Based Year 2 follow-up of AN004T (AN005T)
  - Follow-up trial without new treatments
- EEC Exploratory Dose Ranging (AN008T)
  - AllerT SC N=160 ; Placebo N=53

SC: subcutaneous injection with aluminum hydroxide ; 5 injections over 2 months ; EEC: Environmental Exposure Chamber
Safety and Immunology Proof-of-Concept
AllerT Phase I/IIa (AN003)

- **Safe and immunogenic in clinical phase I/IIa** (AN003)
  - Double-blind, randomized AllerT (N=15) vs placebo (N=5)
  - Allergen-dose equivalent to 3 years of allergy shots
  - Five SC injections on days 1, 7, 14, 21 and 51

### Strong Immune Responses

4 weeks after the last preseasonal injection

- **Baseline = 100**
- **Interleukin-10**
  - Placebo: x9
  - AllerT: x20
- **IgG4**
  - Placebo
  - AllerT: x20

* IgG4: allergen specific immunoglobulin G4

Anergis results from AllerT Phase I/IIa trial AN003
Pellaton *et al.* *Clinical and Translational Allergy* 2013, 3:17
Long-Lasting Immune Memory

Allergen-Specific IgG4 after 2\textsuperscript{nd} and 4\textsuperscript{th} Seasons in the Phase 1 Patients

Data (median) from blood samples collected from subjects allergic to birch pollen who had received 5 SC injections over 2 months of placebo or AllerT 95 µg in trial AN003. All within group changes from baseline for placebo are NS. Placebo N=5, AllerT N=15.
## AllerT Field-Based Phase IIb trials

- Placebo-controlled, double-blind, randomized multicenter trial (AN004T)
- Follow-up second season efficacy trial (AN005T)

### Study Design

<table>
<thead>
<tr>
<th>Subject screening</th>
<th>Pre-seasonal treatment</th>
<th>Birch pollen season Year 1</th>
<th>Birch pollen season Year 2</th>
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</table>

### Eligibility Criteria

Moderate to severe allergy to birch pollen

### Treatments

- **AllerT 100 µg**
- **AllerT 50 µg**
- **Placebo**

### Study Timeline

<table>
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<th>Year 1</th>
<th>Year 2</th>
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### Symptoms Medications

- Quality of Life
- Immunology

### Notes

- *Scheduled doses: half of target dose on Day 1 followed by target dose on days 7, 14, 28 and 56*
AllerT successful field-based trials
Phase IIb Year 1

Clinical Efficacy in conditions required for Product Approval

RSMS during first birch pollen season (AN004T) Year 1 (Median RSMS, mITT set)

Primary Endpoint: RSMS

Nighttime Nasal Symptom Score

Total Score of the Mini-RQLQ (Juniper et al.)

RSMS: Rhinoconjunctivitis Symptom and Medication Score - Mini- RQLQ: validated Rhinoconjunctivitis Quality of Life Questionnaire
AllerT successful field-based trials
Phase IIb Year 2

Sustained Clinical Efficacy in conditions required for Product Approval

RSMS during second birch pollen season (AN005T) Year 2 (Median RSMS, PP set)

RSMS: Rhinoconjunctivitis Symptom and Medication Score
Mini-RQLQ: validated Rhinoconjunctivitis Quality of Life Questionnaire
A 25% Difference from Placebo in Combined Score is Clinically Meaningful

Ragwitek® was approved by FDA in 2014 with 23-25% during the first season

MK-3641 (SCH 039641): RAGWEED ALLERGY IMMUNOTHERAPY TABLET
FDA ADVISORY COMMITTEE MEETING BACKGROUND PACKAGE

<table>
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<tr>
<th>TCS during Peak Season</th>
<th>Favors MK-3641</th>
<th>Favors Placebo</th>
<th>Relative Effect</th>
<th>95% CI</th>
<th>Number of Subjects</th>
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-23% (-32, -15) 644

TCS: “Total Combined Score”

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<th>TCS during Entire RPS</th>
<th>Favors MK-3641</th>
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-25% (-33, -16) 658
AllerT Development Status
Favorable Risk-Benefit Ratio

- **Efficacy proven in conditions of natural exposure**
  - Clinically relevant difference from placebo in combined score in Year 1

- **Sustained efficacy**
  - Seasonal allergy symptom relief maintained during Year 2
  - Significant IgG4 elevations proven until Year 4, naturally boosted by the pollen seasons

- **Safe and well tolerated**
  - 1569 SC injections of AllerT in 335 subjects without anaphylactic shock or grade 3 immediate (< 30 min) systemic allergic reaction
  - Systemic reactions related to the efficacy of AllerT are well manageable

- **AllerT 50 µg is likely to be the optimal dose**
  - 50 µg is clinically as efficacious as 100 µg
  - The increase in allergen-specific IgG4 is lower with 10 µg and 25 µg than with 50 µg
  - ATIBAR registration field trial ongoing, 450 patients, AllerT 50 µg vs 10 µg vs placebo
Ultra-Fast AIT Pipeline Strategy

- Develop lead product candidate through to clinical phase III
- Advance preclinical product candidates to clinical phases
- Discover and develop further product candidates

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- 200-300 pts
- Phase III
- 800-1600 pts
The Future of Allergy Treatment
Ultra-Fast Allergy Immunotherapy

Contact: info@anergis.ch