NEOVACS
LEADER
IN ACTIVE
IMMUNOTHERAPY
FOR THE TREATMENT
OF AUTOIMMUNE DISEASES

2018 CORPORATE PRESENTATION
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AN INNOVATIVE APPROACH TO ACTIVE IMMUNOTHERAPY

<table>
<thead>
<tr>
<th>Company</th>
<th>Listed on Euronext Growth Paris since April 2010 (ALNEV, ISIN: FR0004032746)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Technology</td>
<td>Kinoids®, anti-cytokine therapeutic vaccines. The vaccine uses the patients’ own immune system to regulate inappropriate cytokine overproduction (active immunotherapy). Neovacs’s lead product IFNα Kinoïde is IP protected until 2032</td>
</tr>
<tr>
<td>Therapeutic markets for kinoid technology platform</td>
<td>Three products targeting inflammatory and autoimmune diseases, allergies and cancers: billion dollar markets</td>
</tr>
<tr>
<td>PRODUCTS</td>
<td>IFNα Kinoïde</td>
</tr>
<tr>
<td>INDICATIONS</td>
<td>Lupus</td>
</tr>
<tr>
<td></td>
<td>Dermatomyositis</td>
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<tr>
<td></td>
<td>Type 1 Diabetes</td>
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<tr>
<td></td>
<td>- CKD Pharmaceutical, South Korea</td>
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<tr>
<td></td>
<td>- Biosense Global LLC, China</td>
</tr>
<tr>
<td></td>
<td>- Centurion Pharma, Turkey</td>
</tr>
</tbody>
</table>
KINOIDS®:
A BREAKTHROUGH TECHNOLOGY
Therapeutic vaccine is active immunotherapy

An antigen is injected into patient to induce or amplify a specific immune response

**Today**
Passive Immunotherapy: Monoclonal Antibody

**Tomorrow - the Kinoids**
Active Immunotherapy: Polyclonal Antibodies

**Kinoid technology:**
- Induces a specific immune response in the patient
- Is a therapeutic alternative to treatment with monoclonal antibodies
A VACCINE APPROACH TO TREAT AUTOIMMUNE DISEASES

- Target multiple epitopes: Broad and sustained efficacy
- Blocking of overproduced cytokine, and its pro-inflammatory effects
- Specific to cytokine: no cross-neutralization with other cytokines
- No blocking anti-drug antibodies (ADA)
- T cell tolerance towards the cytokine is NOT broken: no uncontrolled autoimmunity
Kinoid® induces natural polyclonal antibodies: no risk of anti-drug antibody (ADA)

**Kinoid induces binding to multiple epitopes vs. single epitopes (Mabs)**

**IFNα Kinoid:**
- ~1mg of protein/year
  - vs. >1g/year with Mabs

**IFNα Kinoid:**
- 5 injections i.m. the first year, vs. once every 2–4 weeks i.v./s.c. (mAbs)
  - without hospitalization
KINOIDS: AN ADVANCED PIPELINE

<table>
<thead>
<tr>
<th>Study</th>
<th>Preclinical</th>
<th>Phase I</th>
<th>Phase II</th>
<th>Phase III</th>
</tr>
</thead>
<tbody>
<tr>
<td>IFNα Kinoid in Lupus - Europe, LATAM, Asia, U.S.</td>
<td></td>
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<tr>
<td>IFNα Kinoid in Dermatomyositis (DM) – EU, US</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>IFNα Kinoid in Type 1 Diabetes</td>
<td></td>
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<td></td>
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<tr>
<td>VEGF Kinoid in DMLA</td>
<td></td>
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<tr>
<td>VEGF Kinoid in solid tumors</td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>IL-4/IL-13 Kinoid in allergies</td>
<td></td>
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</tbody>
</table>

Study design under evaluation
KINOIDS TARGETING MAJOR THERAPEUTICS MARKET

- Kinoids could address many autoimmune diseases
- A market representing approximately $45 billion in 2022\(^1\).

\(^1\)Estimation Research and Market - September 2017 "Global autoimmune diseases"
Autoimmune diseases are characterized by a dysfunction of the immune system leading to the overproduction of an endogenous cytokine, with no reaction of the immune system.

100 autoimmune diseases\(^1\) including: type 1 diabetes, lupus, dermatomyositis, Alzheimer's disease, multiple sclerosis, etc.

Their prevalence is constantly increasing\(^2\).

Current treatments have no curative effect but major side effects.

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\(^1\)American Autoimmune Related Diseases Association: www.aarda.org

\(^2\)Inserm
IFNα Kinoid :
The most advanced product from Neovacs Research and Development
## A STRONG INTERNATIONAL IP PROTECTION FOR IFN\(\alpha\) KINOIDE UNTIL 2032

<table>
<thead>
<tr>
<th>Pat.#</th>
<th>Nature of Patent</th>
<th>Country</th>
<th>Exp. Date</th>
</tr>
</thead>
<tbody>
<tr>
<td>WO/2012/136739</td>
<td>Use/method</td>
<td>CN, US, RU, EP, AU, MX, HK</td>
<td>2032</td>
</tr>
</tbody>
</table>

### Patent in prosecution

<table>
<thead>
<tr>
<th>Pat.#</th>
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<tbody>
<tr>
<td>WO/2012/136739</td>
<td>Use/method</td>
<td>CA, JP, BR, IL, IN, KR</td>
<td>2032</td>
</tr>
</tbody>
</table>
Robust scientific evidence confirms the major role of IFNα in the dysfunction of the immune system in patients with autoimmune diseases such as lupus\(^1\), dermatomyositis\(^2\) and type 1 diabetes\(^3\).

Lupus patients have high serum levels of IFNα and/or overexpress genes induced by type I interferons \(^4\).

\(^1\)Crow et al., Translat Res 2015, \(^2\) Greenberg et al. Genes and Immunity 2012, \(^3\) Lehuen et al., 2013, \(^4\)Chiche et al., Arthritis Rheum,
LUPUS, A RARE DISEASE WITH MULTIPLE SYMPTOMS

- A chronic and debilitating disease
- The disease affects mostly women (9 women/1 man).
- Lupus is characterized by periods of flares alternating with periods without symptoms (remissions)
- The onset age of the disease is between 15 and 45 years old
- The number of patients worldwide is estimated at 5 million \(^{(1)}\).
- No curative therapy

\(\text{(1)}\) FAI2R and Lupus Foundation of America

Celebrities suffering from lupus
Selena Gomez (Singer), Seal (Singer)
The current background therapy is based on:

- Immunosuppressive agents: Corticosteroids, Methotrexate, azathioprine, ...
- Hydroxychloroquine
- Monoclonal Antibody (Benlysta®)
- « Pain-killers » and non steroids anti-inflammatory

Available treatments aim to reduce inflammation and associated pain to address the disease’s main symptoms and prevent complications, but with serious adverse effect over time
Clinical program for IFNα kinoid in lupus: phase I/IIa and phase IIb
METHODOLOGY AND POPULATION OF PHASE I/IIa STUDY

Study completed

Objectives

- Safety
- Immune responses
- Neutralization of IFN-alpha- and SLE- dysregulated genes

Population

- 18-50 years
- SLE ACR 4/11
- SLEDAI 4-10
- ANA and/or anti-dsDNA positive
- Corticosteroid ≤ 20mg/day
- No BILAG A

Design

- (Double-blind, placebo controlled, 3:1 (IFN-K/Placebo)
- 28 pts, 7 countries, 12 centers
- Staggered dose increase
  - Kinoid 30 mcg/dose vs placebo
  - Kinoid 60 mcg/dose vs placebo
  - Kinoid 120 mcg/dose vs placebo
  - Kinoid 240 mcg/dose vs placebo
- Schedule of administration
  - 3 IM injections, D0-D7-D28
  - 4th dose at week 12 in 50% of patients for groups at 60,120,240 mcg

ClinicalTrials.gov Identifier: NCT01058343
6 MONTHS RESULTS:
100% PATIENTS DEVELOP ANTI-IFNα ANTIBODIES

Increasing doses and number of injections of IFNα Kinoid led to increased anti-IFNα responses, and neutralizing capacity response to IFNα

Source: Lauwerys et al, 2013, Arthritis & Rheum
A strong neutralizing capacity of anti-IFNα Ab induced by IFN-K administration

<table>
<thead>
<tr>
<th>IFNα Sub-type 10 U/mL</th>
<th>Polyclonal antibodies of an IFN-K immunized Patient (D964) (Dilution)</th>
<th>9F3 Monoclonal Antibody anti-IFNα (concentration ng/mL)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A 2a</td>
<td>1/22 475</td>
<td>&lt;7,8</td>
</tr>
<tr>
<td>B2</td>
<td>1/8 936</td>
<td>98</td>
</tr>
<tr>
<td>C</td>
<td>1/8 857</td>
<td>&gt;1 000</td>
</tr>
<tr>
<td>D</td>
<td>1/9 648</td>
<td>&gt;1 000</td>
</tr>
<tr>
<td>F</td>
<td>1/2 493</td>
<td>329</td>
</tr>
<tr>
<td>G</td>
<td>1/10 693</td>
<td>78</td>
</tr>
<tr>
<td>H2</td>
<td>1/9 147</td>
<td>57</td>
</tr>
<tr>
<td>I</td>
<td>1/13 354</td>
<td>&gt;1 000</td>
</tr>
<tr>
<td>J1</td>
<td>1/5 270</td>
<td>&gt;1 000</td>
</tr>
<tr>
<td>K</td>
<td>1/16 878</td>
<td>&gt;1 000</td>
</tr>
<tr>
<td>4b</td>
<td>1/10 154</td>
<td>&gt;1 000</td>
</tr>
<tr>
<td>WA</td>
<td>1/10 148</td>
<td>945</td>
</tr>
<tr>
<td>A 2b</td>
<td>1/22 326</td>
<td>&lt;7,8</td>
</tr>
</tbody>
</table>

*TO THE EXTENT THAT ALL IFNα SUBTYPES ARE INVOLVED IN THE ACTIVITY OF SLE

9F3 : mAb deposited at ATCC by Genentech (in 2001 U.S. patent 7,087,726 B2)

Neutralized sub-types

- 13/13
- 2/13 : +++
- 5/13 : +
6 MONTHS RESULTS: TOLERANCE AND ANTI-IFNα ANTIBODIES BIOLOGICAL ACTIVITY

- An acceptable safety profile at the doses inducing an immune response
- Anti-IFNα antibodies significantly higher in lupus patients with a positive IFNα signature at baseline
- Anti-IFNα antibodies significantly correlated with biological markers of disease activity:
  - IFNα signature decrease
  - C3 complement increase

![Graphs and data](Lauwerys et al. Arthritis & Rheumatism 2013)
LONG TERM RESULTS:
PERSISTENCE OF BIOLOGICAL ACTIVITY AFTER STOPPING THE VACCINATIONS

- Neutralizing antibodies persist up to 4 years after the first immunization
- Neutralizing antibodies maintain the normalization of the IFNα signature
- Long-term tolerance, with no severe infection
- The selection of treatment doses and the schedule of administration for phase IIb

J. Ducreux, et al, Rheumatology 2016; IFNα-Kinoid (IFN-K) induces neutralizing anti-IFNα antibodies that decrease the expression of IFN-induced and B cell activation associated transcripts: Analysis of extended follow-up data from the IFN-K Phase I/IIa study
### METHODOLOGY AND POPULATION OF CLINICAL PHASE IIb STUDY

**Objectives**

**Primary end-points:**
- Decrease of IFNα gene signature (biological criteria) and Clinical Efficacy evaluated at Month 9

**Secondary end-points:**
- SRI-4 response
- Lupus flares
- Other clinical criteria, such as “CS tapering”, SF36, FACIT....
- Immune Response exploration

**Population**

- 18-65 years of age
- ACR LED 4/11
- SLEDAI ≥ 6
- AAN et/ou anti-dsDNApositits
- Corticosteroid ≤ 20 mg/day
- Moderate to severe
- with elevated IFN gene signature at baseline

**Design**

- Proof of Concept study, Single-blind, placebo controlled, 1:1 (IFN-K/Placebo)
- 185 patients, 25 countries, 100 centers
- Dosing regimen
  - IFN-K 240 mcg/dose vs placebo Day 0-Day 7-Day 28
  - IFN-K 120 mcg/dose vs placebo Month 3-Month 6 (booster)

ClinicalTrials.gov Identifier: NCT02665364

Recruitment completed
A STUDY APROVED WORLDWIDE

USA
100/100,000 population prevalence

EUROPE
50/100,000 population prevalence

AFRICA
100/100,000 population prevalence

LATAM
80/100,000 population prevalence

ASIE
50/100,000 population prevalence
Official scores for clinical study in lupus:

- **BICLA et SRI-4**, these 2 scores are validated by all the international health authorities, to evaluate the clinical response in clinical studies targeting lupus.

- These two scores are registrable to the health authorities (1).

Benchmark of other phase IIb clinical studies in lupus:

<table>
<thead>
<tr>
<th>Source</th>
<th>Definition of response</th>
<th>Time</th>
<th>Active</th>
<th>Placebo</th>
<th>Difference</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Belimumab IV²</td>
<td>SRI(4) from pooled BLISS-76 &amp; -52 studies</td>
<td>1 year</td>
<td>50.6%</td>
<td>38.8%</td>
<td>11.8%</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Belimumab SC³</td>
<td>SRI(4)</td>
<td>1 year</td>
<td>61.4%</td>
<td>48.7%</td>
<td>12.7%</td>
<td>0.001</td>
</tr>
<tr>
<td>Anifrolumab⁶</td>
<td>SRI(4) and oral CS reduction: Total</td>
<td>W24</td>
<td>34.3%</td>
<td>17.6%</td>
<td>16.4%</td>
<td>0.014</td>
</tr>
<tr>
<td>High IFN signature</td>
<td>W24</td>
<td></td>
<td>36%</td>
<td>13.2%</td>
<td>22.8%</td>
<td>0.004</td>
</tr>
<tr>
<td>Low IFN signature</td>
<td>W24</td>
<td></td>
<td>29.2%</td>
<td>30.8%</td>
<td>- 1.6%</td>
<td>0.946</td>
</tr>
<tr>
<td>SRI(4) and oral CS reduction: Total</td>
<td>1 year</td>
<td>51.5%</td>
<td>25.5%</td>
<td>26.0%</td>
<td></td>
<td>0.047</td>
</tr>
<tr>
<td>High IFN signature</td>
<td>1 year</td>
<td>52.0%</td>
<td>19.75%</td>
<td>32.3%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Low IFN signature</td>
<td>1 year</td>
<td>50%</td>
<td>42.3%</td>
<td>7.7%</td>
<td></td>
<td>0.514</td>
</tr>
<tr>
<td>BICLA</td>
<td>1 year</td>
<td>53.5%</td>
<td>25.7%</td>
<td>27.8%</td>
<td></td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

### Lupus Market Overview

- **5-6 millions patients worldwide**\(^{(1)}\)
- **Improving information and the quality of healthcare services promote diagnosis**

<table>
<thead>
<tr>
<th>Product</th>
<th>Status</th>
<th>Technology</th>
<th>Price</th>
</tr>
</thead>
<tbody>
<tr>
<td>Benlysta® (GSK)</td>
<td>Status: registered as &quot;add-on&quot; treatment, indicated in adult patients with active systemic lupus with presence of autoantibodies and high disease activity.Technology: Anticorps monoclonal, Price: $30,000/year in U.S.(^{(1)})</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anifrolumab (Astrazeneca)</td>
<td>Status: Phase III, Technology: Monoclonal Antibodies targeting type 1 IFNα receptor. Price: no indication yet</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Estimated growth in lupus drug sales would rise from $1 billion in 2015 to $2.9 billion in 2025 in the top 7 markets**\(^{(3)}\)

\(^{(1)}\) Lupus Foundation of America  
\(^{(2)}\) According to "Decision Resources 2016" research  
\(^{(3)}\) According to "Global Data 2017"
IFNα kinoid is a breakthrough therapeutic approach, which aims to meet the needs of patients, medical community and healthcare systems:

- A long-term effect
- A less constraining posology
- Steroid-sparing: fewer long-term adverse effects
- A favorable safety profile
- A favorable pharmaco-economic profile
### STRATEGIC PARTNERSHIPS IN U.S., EUROPE AND CHINA

<table>
<thead>
<tr>
<th>TYPE</th>
<th>PRODUCTS</th>
</tr>
</thead>
<tbody>
<tr>
<td>COMMERCIAL &amp; OUT-LICENSING</td>
<td>▪ IFNα KINOID – LUPUS &amp; DM</td>
</tr>
<tr>
<td></td>
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</tr>
<tr>
<td>INDUSTRIAL</td>
<td>▪ IFNα KINOID</td>
</tr>
<tr>
<td>ACADEMIC</td>
<td>▪ IFNα KINOID- TYPE 1 DIABETES</td>
</tr>
<tr>
<td></td>
<td>▪ VEGF KINOID- OVARIAN &amp; COLORECTAL CANCER</td>
</tr>
</tbody>
</table>
NEOVACS INITIATES PHASE IIB STUDY IN LUPUS WITH IFNα KINOID

NEOVACS OBTAINS IND APPROVAL FROM THE U.S. FDA to extend its Phase Ib clinical trial in lupus to United States

NEOVACS GRANTED FDA “FAST TRACK” DESIGNATION for IFNα Kinoid in lupus (SLE)

END OF RECRUITMENT FOR THE PHASE IIB STUDY IN LUPUS WITH IFNα KINOID

FINAL RESULTS OF PHASE IIB STUDY WITH IFNα KINOID IN LUPUS
Key milestones following positive results from the Phase IIb clinical study in lupus with IFNα kinoid:

- Finalize discussions for a global partnership with the IFNα Kinoid in lupus and DM according to the usual terms for this kind of agreement.

- Validate with the healthcare authorities the lupus Phase III clinical program.

- Submit an ODD request in South Korea, as agreed with our partner CKD.
OLIVIER DHELLIN
Directeur du développement pharmaceutique
- Docteur en pharmacie (Université Paris XI, France) et PhD en virologie (Université Pierre et Marie Curie, France).

BERNARD FANGET
VP Affaires pharmaceutiques
- Diplômé de biochimie de l’Université de Lyon, France.

NATHALIE THOMAS-PUJOL
Directrice des affaires réglementaires
- Nathalie a rejoint Néovacs en 2014 après plus de 20 ans dans l’industrie pharmaceutique, notamment en tant que directrice des affaires réglementaires Europe, Moyen-Orient et Afrique chez Cephalon/Teva. Avant cela, elle a travaillé près de 15 ans chez Sanofi-Aventis R&D.
- Doctorat de pharmacie de l’Université de Rouen, complété d’un PhD en toxicologie de l’Université de Paris VII.

THERESE CROUGHS
Chief Medical Officer
- Thérèse a rejoint Néovacs en 2015. Auparavant CMO de Cytheris, directrice de la BU Lauriad & NCE chez Onxeo (précédemment BioAlliance Pharma), et conseillère médicale internationale sur les développements cliniques en Europe du NovoSeven® (r-FVIIa) pour le traitement des hémorragies sévères chez Novo Nordisk. Thérèse Croughs a été chef de projet international pour le Kogenate® (r-FVIII) pendant 10 ans chez Bayer.
- Diplômée de la faculté de médecine de l’Université Catholique de Louvain, Belgique.

Baptiste Pourtout
Directeur Financier

GÉRALDINE GROUARD-VOGEL
Directrice scientifique
- Géraldine a rejoint Néovacs en 2005. Elle a auparavant travaillé chez Sanofi Pasteur États-Unis dans le développement de vaccins bactériologiques, et en tant que chercheuse au Walter Reed Army Institute of Research, ainsi qu’à l’université de Seattle.
- Docteur en pharmacie de l’Université d’Angers (France) et PhD en immunologie avec le Pr. Jacques Banchereau de Schering-Plough Lyon (France).
Prof. JACQUES BANCHEREAU, PhD
Président du CSI
• Directeur du département de sciences immunologiques au Jackson Laboratory for Genomics Medicine, University of Connecticut Health Center
• Baylor Institute for Immunology Research, Dallas, Texas, États-Unis

Prof. BETTY DIAMOND, MD
• Investigateur principal, Center for Autoimmune and Musculoskeletal Diseases, The Feinstein Institute for Medical Research
• Professeur de médecine moléculaire et de médecine, Hofstra North Shore-LIJ School of Medicine, Manhasset, NY, États-Unis

Prof. NAPOLEONE FERRARA, MD
• Professeur émérite de pathologie et professeur émérite adjoint d’ophthalmologie
• Directeur des sciences fondamentales, UC San Diego Health System - La Jolla, CA, États-Unis

Prof. MIRIAM MERAD, MD, PhD
• Professeure de sciences oncologiques et de médecine, Tisch Cancer Institute, New York, États-Unis
• Directeur du Human Immunomonitoring center, Tisch Cancer Institute, New York, États-Unis
• En 2013, le Dr Merad a été l’organisatrice principale du prestigieux symposium Keystone sur la biologie des cellules dendritiques

Prof. LAURENCE ZITVOGEL, MD
• Directrice de recherche à l’INSERM U1015, centre de lutte contre le cancer Gustave Roussy
• Centre d’investigation clinique biothérapie (CICBT) 507, Villejuif, France

Prof. MIRIAM MERAD, MD, PhD
• Professeure de sciences oncologiques et de médecine, Tisch Cancer Institute, New York, États-Unis
• Directeur du Human Immunomonitoring center, Tisch Cancer Institute, New York, États-Unis
• En 2013, le Dr Merad a été l’organisatrice principale du prestigieux symposium Keystone sur la biologie des cellules dendritiques

Dr. VIRGINIA PASCUAL
• Directrice, Center for Inflammation and Autoimmune Diseases
• Directrice, Center for Personalized Medicine
• Professeure adjointe de pédiatrie, University of Texas Southwestern Medical Center, Dallas, Texas, États-Unis
• Professeure adjointe de pédiatrie, Mount Sinai School of Medicine, New York, États-Unis
• Professeur agrégé adjoint en études biomédicales, Baylor University

Prof. BERNARD LAUWERYS, MD, PhD
• Unité de rhumatologie, SSS/IREC/RUMA, cliniques universitaires Saint Luc & université catholique de Louvain, Bruxelles, Belgique