A new KEY to a global portfolio
MESSAGE
From Roberto Gradnik, CEO

WIDER VIEW
International expansion gathers pace

FOCUS
Oralair® key to a global portfolio

FOCUS
Targeting house dust mite allergies

REPORT
House dust mite breeding under control
AN EVOLVING COMPANY

STALLERGENES is an international biopharmaceutical company dedicated to allergen immunotherapy for the treatment of respiratory allergic diseases such as rhinoconjunctivitis, severe rhinitis and allergic asthma.

IN 50 YEARS OF OPERATION, Stallergenes has greatly contributed to the development of allergen immunotherapy (AIT) and today retains the same commitment to innovation.

Leaving global pharmaceutical producer of house dust mites and grass pollen.

IN 2012 = SALES IN MILLIONS OF EUROS

IN 50 YEARS = SALES IN MILLIONS OF EUROS

88% OF SALES = SUBLINGUAL IMMUNOTHERAPY

500,000 PATIENTS TREATED EVERY YEAR BY STALLERGENES

MORE THAN 1,000 EMPLOYEES

240 = SALES IN MILLIONS OF EUROS

IN 50 YEARS OF OPERATION

APPROXIMATELY 20% OF REVENUE INVESTED EACH YEAR IN R&D

PERSONALISED MEDICINE: 3.5 MILLION BOTTLES PRODUCED EACH YEAR
200 MILLION EUROS INVESTED IN R&D IN 5 YEARS

3,000 NPP* PRESCRIPTIONS PROCESSED EVERY DAY
* Named Patient Products

38% of 2012 growth generated by new international markets

50% + OF GRASS POLLEN NEEDS MET OVER TIME BY OUR PRODUCTION OF RAW MATERIALS

€15 M INVESTED EVERY YEAR IN PRODUCTION

ORALAIR®: The AIT tablet experiencing the fastest growth

43% MARKET SHARE *
* within the same geographic scope in the AIT tablet market at the end of 2012 - IMS data.

10.4% AVERAGE GROWTH 2007-2012

ORALAIR 1ST AIT TABLET ACCEPTED FOR REVIEW BY THE FDA IN THE US

PRODUCTS MARKETED IN OVER 50 COUNTRIES, 18 SUBSIDIARIES INCLUDING 8 CREATED IN THE LAST TWO YEARS
This year, we have once again achieved sales growth and a high level of profitability.

Roberto Gradnik, Chief Executive Officer
A CLEAR STRATEGY

2012 was a year centred on structuring our company for the future. We achieved major milestones for our flagship innovation, Oralair®, the sublingual immunotherapy tablet for the treatment of grass pollen allergies, which was successfully launched in several major markets such as France, Australia, Russia and Canada.

In the United States, the FDA (Food and Drug Administration) agreed to assess the biological product application request (BLA - Biologics License Application) for Oralair®. Development of our second major innovation for allergic rhinitis, the house dust mite immunotherapy tablet, has continued in Europe and Japan, and will shortly begin in the United States. It is also undergoing clinical development for asthma, where significant unmet therapeutic needs exist.

2012 was also the year in which we developed our strategic vision that will take us into a new era, with the aim of becoming a global leader in the fight against allergies through immunotherapy. This vision is built on 3 main areas:
- strengthening our core business, allergen immunotherapy for the treatment of allergic rhinitis, and in parallel, forging ahead with our international expansion;
- developing immunotherapy for the treatment of asthma;
- in the longer term, exploring the relevance of immunotherapy to other allergies (food allergies, drug allergies, etc.).

The implementation of this strategic vision has already shown initial concrete results. Despite the economic crisis facing Europe and its impact on the buying power of both patients and paying organisations, we have again achieved sales growth and a high level of profitability during the 2012 financial year. This growth was driven by new international markets that have performed solidly and represent real sources of future growth for the Group, their sales having increased 28% over the course of 2012. Sales growth will be bolstered by the strength of these new international markets and should accelerate beyond 2013.

We achieved major milestones for our flagship innovation, Oralair®, which was successfully launched in several major markets.
The Board of Directors of Stallergenes, chaired by Patrick Langlois since 1 July 2012, is made up of 12 members.

Patrick LANGLOIS
Chairman of the Board
Managing Partner of PJL Conseils

Roberto GRADNIK
Chief Executive Officer of Stallergenes

Jean-Luc BELINGARD
Chairman and CEO of BioMérieux

Jean BOUSQUET
Full Professor in Respiratory Illness Department, Arnaud de Vileneuve Hospital, Montpellier

Maria-Gabriella CAMBONI
Chief Operating Officer, EOS

Christian CHAVY
Partner, Ares Life Sciences

Michel DUBOIS
Former Secretary General of Institut Mérieux

Patrick LEE
Partner, Ares Life Sciences

Stephan MEISTER
Group Chief Operating Officer, Waypoint Capital

Paola RICCI
Partner, Ares Life Sciences

Albert SAPORTA
Former Chairman and CEO of Stallergenes

Jacques THEURILLAT
Partner, Ares Life Sciences
Stallergenes’ management team, gathered around Roberto Gradnik, Chief Executive Officer, is made up of 13 people who manage the major functions of the company, and who are involved in strategic planning and coordinating cross-departmental processes.

Executive Committee (at 30 April 2013)

1. Paul-Louis Gayrel
   Senior VP, Regulatory and Compliance

2. Cécile Hilaire
   Senior VP, Strategic Marketing and Market Access

3. Poul Sorensen
   Senior VP, Strategic Development

4. Robert Zeldin
   Senior VP, Global Clinical Development

5. Pierre Catignol
   Senior VP, Industrial Affairs

6. Roberto Gradnik
   Chief Executive Officer

7. Cyril Tavier
   Senior VP, Southern Europe Operations

8. Philippe Munding
   Senior VP, Research and Pharmaceutical Development

9. Olivier de Beaumont
   Senior VP, Global Medical Affairs

10. Thomas Lang
    Senior VP, General Manager US

11. Richard Lejosne
    Senior VP, Human Resources

Philippe Verrez
Senior VP, International Operations (not present)

Peter Buhler
Chief Financial Officer (not present)
After 50 years in operation, Stallergenes is at a turning point in its history: with a new strategic vision, the company has the resources to become the global leader in allergen immunotherapy.

A VISION SHAPING TOMORROW’S LEADER

INTERVIEW WITH:

PATRICK LANGLOIS
Chairman of the Board of Directors

ROBERTO GRADNIK
Chief Executive Officer
A little more than a year after your arrival at the head of Stallergenes, how would you assess the Group’s performance in 2012?

Roberto GRADNIK: In terms of performance, in 2012 Stallergenes achieved an increase of 3.2% in consolidated sales compared with the previous year, and maintained a high level of profitability. The operating profit stood at €69.3 million, up 7.9%, and made up 28.9% of sales. At the end of 2012, we had a net cash position of €90.4 million, which will be used to support our international expansion and our clinical development programmes.

Looking beyond these positive signs, Stallergenes is at a pivotal stage in its development. The company has invested in new international markets, thereby basing its activity on sources of growth that will make up for the stagnation in the European market. Stallergenes has the potential to meet the challenges of having a strong global presence, of gaining market share, of the marketing of Oralair® in the United States and the development of asthma treatments.

Stallergenes has the potential to meet the challenges of having a strong global presence.

— Roberto Gradnik

What have been the main strides forward made with the roll out of Oralair®?

Patrick LANGLOIS: Our sublingual immunotherapy tablet for grass pollen Oralair® has strengthened our position and allowed us to reach new markets. Oralair® is made up of five grass pollen extracts that correspond to the epidemiological characteristics that patients are exposed to and uses an intermittent protocol.

R.G: This product is now available in 20 countries and saw its sales increase by 33% in 2012, reaching €16.2 million. The launch of Oralair® in France at the end of 2012 worked very well and will, in the future, enable this growth to accelerate further. Outside Europe, after its successful launch in Australia and New Zealand in May, Oralair® was launched in Russia and Canada in October 2012, recording the first sales of an immunotherapy tablet in North America.

In the United States, the FDA agreed in February 2013 to assess our biological product application request (BLA - Biologics License Application) for Oralair, thereby making Stallergenes the first pharmaceutical company to have its submission of an application request for a sublingual immunotherapy tablet in this market accepted for assessment by the FDA.

How is the development of the sublingual immunotherapy tablet for house dust mite allergies progressing?

R.G: We are continuing the development of this tablet, which will involve the 3 major global regions: Europe, the United States and Japan. In the United States, a phase III clinical study will soon be launched. In Japan, clinical development, initiated by our partner Shionogi, is underway with a phase II/III study. At the same time, we launched our asthma development programme and in 2012, carried out a phase I study that confirmed the tolerance data of our tablet taken in high doses. A phase II study is under development.

What is your business outlook for 2013?

P.L: There will be slight growth in the business in 2013. Whilst Europe will experience limited growth, the new international sources of growth will make a greater contribution to overall performance. Sales growth will be boosted by the strength of these markets and should accelerate beyond 2013.

R.G: Beyond this year, a new source of growth will emerge due to the upcoming launch of Oralair in the United States, scheduled for the first quarter of 2014.
In 2012, the global allergic rhinitis market was estimated to be €4.5 billion. Allergen immunotherapy makes up 19%, or €845 million, of this market, an increase of 3.3% compared to 2011.

The allergen immunotherapy market has historically been European, where this therapy has been developing steadily since its discovery at the start of the 20th century, despite great disparities from one country to another and a low penetration rate overall, in the order of 10%. In 2012, the European immunotherapy market experienced a slowdown, mainly due to the economic crisis, which has affected many European Union countries since 2008. Southern Europe (Italy and Spain) has been particularly affected, with sales falling 13% and 5% respectively.

A STRONG IMPACT ON HEALTH EXPENDITURE
The economic and financial crisis and increased budgetary constraints have put additional pressures onto the health systems of many European countries. Several of them, notably those hardest hit by the crisis, have taken a series of measures to reduce their public health spending. In 2010, the increase in real terms in per capita health expenditure slowed or decreased in almost every European country, thereby reversing the trend of continued growth. Whilst the reduction in expenditure was already underway in 2009 in countries hit hardest by the economic and financial crisis, even bigger restrictions took effect in 2010 in the face of increased budgetary pressures and growing debt burdens. Within the European Union, per capita health spending rose on average by 4.6% annually in real terms between 2000 and 2009, before falling by 0.6% in 2010. Public health spending has been reduced through a series of measures to reduce their public health spending.

INTernational expansion gathers pace

Dust mites (%): 51%
Grasses (%): 49%
Ragweed (%): 49%
Birch (%): 28%

Public spending growth slowed down or even declined in many European countries.

USA: A real need for an innovative sublingual treatment

Under the care of around 10,000 specialists, 2.8 million patients are today being treated by allergen immunotherapy, although this only accounts for 5% of America’s allergic population. The current practice of immunotherapy in the United States consists of multiple injections carried out under medical supervision. There is a real need for an innovative sublingual treatment in this country, since approved allergen immunotherapy is currently not available for self-administration by patients.
In the United States:

- 49% of respiratory allergies are caused by grass pollen

In Japan:

- 90% Japanese cedar (commonly known as Japanese cedar)
- 50% Dust mites
- 27% Birch

Japan: a huge opportunity to be seized in concert with our partner Shionogi

In order to respond to the high demand for allergy treatments in Japan, Stallergenes is counting on the partnership deal agreed with Shionogi, which is progressing very well. The sublingual immunotherapy tablet for dust mites, which is currently the subject of a phase II/III clinical study, will be the first product launched on the Japanese market, followed by the tablet for Japanese cedar pollen.

In Europe, the Springboard for International Expansion

Stallergenes has a core base in European markets that currently makes up 85% of its annual sales. The company has a strong foothold in the main European immunotherapy markets. The economic crisis experienced by Europe and its impact on the buying power of patients and paying organisations has had an effect on Stallergenes’ sales, particularly in Southern Europe. Today the Group is looking to consolidate its position in major markets such as Germany, and is continuing its development in new European markets.

EUROPE, THE SPRINGBOARD FOR INTERNATIONAL EXPANSION

 measures, including a reduction in salaries and/or jobs, an increase in direct household payments for certain services and pharmaceutical products and the imposition of significant budgetary constraints on hospitals. As a result of the negative growth of health expenditure in 2010, the share of GDP allocated to this sector has levelled out or dipped slightly in many EU member states.

In 2010, the European Union member states allocated on average (non-weighted) 9% of their GDP to health expenditure, lower than the 9.2% level reached in 2009.
Thus in 2011-2012 Stallergenes set up new subsidiaries in the United Kingdom and Poland. In addition to consolidating its position in Europe, Stallergenes anticipated the slowdown in growth in these markets and identified new sources of growth that showed initial signs of success in 2012.

NEW INTERNATIONAL MARKETS DRIVING GROWTH
Today Stallergenes covers 86% of the global market and has opened 8 new subsidiaries since 2011, including 5 in new international markets (Argentina, Australia, Jordan, Russia and Turkey). These new markets contributed 38% to Stallergenes’ growth in 2012, as against 9% en 2011.

THE UNITED STATES IN SIGHT
In the United States, following the FDA’s agreement to examine the BLA request for Oralair, Stallergenes is assessing how to best market this product, with the aim of rapidly making a strong impact on the American market. Potential collaborations with companies operating in the allergy field are under consideration, and in particular with Greer Laboratories Inc., the US market leader in immunotherapy and Antigen Laboratories Inc., which were both acquired by Ares Life Sciences.

Interview with Alexei Pyatkov, Managing Director of the Russian affiliate

What potential does the Russian market represent for Stallergenes?
Russia is a dynamic and developing country with a large population (143 million people) with an allergy prevalence rate similar to other European countries and a very low allergen immunotherapy penetration rate (about 2% of eligible patients). As the only global player in this market, Stallergenes has the ability to harness this potential and to become the go-to AIT company for Russian allergists.

How can Stallergenes cover a country as huge as Russia?
Our coverage is progressing steadily. We already cover one third of the population, concentrating on the 20 largest cities. In 2012, we doubled the number of physicians visited, which represents two thirds of the total number of allergists practising in Russia.

What are the Russian affiliate’s initial results?
We have experienced a lot of interest and enthusiasm from Russian allergists, in particular in immunotherapy and our new innovative sublingual products. Sales are growing accordingly. 2012 sales trebled compared to 2011. Within a few years, we are confident that Russia will represent a sizeable part of Stallergenes’ sales. Just two months after the launch of Oralair®, we have already taken on nearly 1,000 patients in this country.
Marketed in Germany since 2008, Oralair® has been rolled out gradually, firstly in Europe, then in new international markets with strong potential. To date, this medicine is available in 20 countries.

**ORALAIR®, THE KEY TO A GLOBAL PORTFOLIO**

A CONCENTRATION OF EXPERTISE AND EFFICACY

Stallergenes’ sublingual grass pollen immunotherapy tablet Oralair® is used for the treatment of respiratory allergies caused by grass pollen. Having been the subject of five phase III clinical studies on more than 1,800 patients in Europe, Oralair® has demonstrated both its short and long-term efficacy. It has also been the subject of a Phase III study in adults in the United States, whose results are consistent with those obtained in Europe. Oralair® is unique, consisting of five grass pollen extracts that correspond to the epidemiological characteristics that patients are exposed to. As grass pollen allergy is seasonal, this treatment is taken for a few months of the year, before and during the pollen season. In Europe, Oralair® is marketed in 16 countries, including France since December 2012. This launch represents a major challenge, as France is the second largest European immunotherapy market, after Germany. Thanks to its composition and its intermittent protocol, Oralair® has rapidly gained market share in France. The product is also continuing its expansion beyond Europe:

Oralair® achieved a 43% market share in the tablet segment.

*within the same geographic scope
In the AIT tablet market at the end of 2012 IMS data
**2012-2013 highlights**

**LAUNCH**

in Australia, Russia, Canada and France

Agreement by the FDA to assess the BLA request for Oralair

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**ORALAIR® - FIRST STEPS IN THE AMERICAN MARKET**

In Canada, respiratory allergies are estimated to affect around 20%-25% of the adult population, with around half of those being sensitive to grass pollen. Treatment of grass pollen allergies by immunotherapy is administered by multiple allergen injections, according to a pre and co-seasonal or perennial protocol. In 2007, Stallergenes established a partnership agreement with the Canadian company Paladin Labs Inc.

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**Interview with Dr. Sophie Silcret-Grieu, a consultant allergist based in Paris.**

As an allergist, what are your thoughts on the immunotherapy tablet Oralair® that was launched in France at the end of 2012?

I have been practising immunotherapy for a long time with solution-based treatments, which are made up of the same 5 grasses pollens and use the same pre and co-seasonal protocol. Allergists recognise the significance of both this composition and this protocol. The efficacy and tolerance of the tablet are both well established. I see Oralair® as an improvement as it simplifies both the treatment and the prescription process.

What advantages do you see for patients?

Taking Oralair® is very simple, helping to avoid handling mistakes which can sometimes occur with solution-based treatments. An ability to be stored at room temperature means the treatment can be followed more easily.

As there is a very short time between the prescription and obtaining the medication, the patient can easily remember how to take the treatment. Saving time in this way gives the option of starting a course of treatment over a longer period, and so it allows patients who consult their allergist belatedly to be treated as well.

Oralair offers ease of use to both physicians and patients.

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After being launched in May 2012 in Australia and New Zealand, it has been on sale for a few months in Russia and Canada. In Russia, Oralair® has large growth potential. In Canada, Oralair® is the first allergen immunotherapy tablet to be registered and marketed in North America.
Thanks to this partnership, Canadian patients are benefitting from a significant advance in the treatment of respiratory allergies due to the introduction of sublingual immunotherapy, and more specifically, to the launch of the Oralair® specialty.

Following the launch in Canada, another milestone was reached in North America, after the FDA agreed in February 2013 to assess the biological product application request (BLA - Biologics License Application) for Oralair. This BLA submission represents a significant step towards the future launch of Oralair on the American market and makes Stallergenes the first pharmaceutical company to have its application request submission for a sublingual immunotherapy tablet accepted for assessment by the FDA.

Interview with Professor Gordon L. Sussman, Professor of Medicine, University of Toronto Acting Division Director, Allergy and Clinical Immunology, University of Toronto, Canada

What will Oralair® offer to Canadian patients?
Oralair® is a real alternative to subcutaneous immunotherapy, particularly as it can be taken at home by the patient for the treatment of seasonal grass pollen allergies.

According to physicians, what advantages does Oralair® offer?
As for any immunotherapy treatment, Oralair® should only be prescribed by physicians properly trained in the treatment of allergic illnesses. Whilst allergy specialists are open to new treatments, it will take time for them to fully appreciate the benefits of this product. They already see Oralair® as a real innovation and a complement to existing therapies, which will enable them to treat a larger number of patients and to better meet their needs. Oralair®’s efficacy has been demonstrated through several placebo controlled clinical trials in Europe and North America, which reinforce our confidence in this new medicine. The pharmacological effect of Oralair® is of interest, as well as the long-term efficacy of immunotherapy. Its five-grass pollen composition covers the most prevalent allergens in Canada. Lastly, its administration fits the seasonality of grass pollen allergies in Canada.
The house dust mite is a universal allergen. More than 40 different species exist, it is found in every part of the world and is the main cause of respiratory allergies: Allergic rhinitis caused by house dust mites affects around 50% of patients suffering from a respiratory allergy in the main areas of the developed world (13).

TARGETING DUST MITE ALLERGY

Most patients suffering from a house dust mite allergy have persistent symptoms throughout the year, and tend to be resigned to their condition (14). Nevertheless, the quality of life of patients suffering from allergic rhinitis caused by house dust mites is severely impaired: patients often experience sleep disturbance, leading to tiredness, irritability, memory problems, daytime fatigue and depression (15), as was shown as part of a perception survey of 4,016 people carried out in four European countries in 2012 (Germany, Spain, France, Italy).

ALLERGEN EXPERTISE WHICH LED TO HIGH DOSAGE DEVELOPMENT

With a wealth of experience of this allergen, Stallergenes is developing high dosage medication for the treatment of house dust mite allergies. Stallergenes has produced its own raw materials for more than 20 years and is now the leading global pharmaceutical producer of house dust mites, producing a tonne every year. Stallergenes, is the global leader in pharmaceutical house dust mite production, thanks to the development of the Stalmite APF® (Animal Protein Free) culture medium, which relies on a feeding standard of house dust mites free of animal and human proteins, based on amino acids and plant based extracts, in optimal temperature and humidity conditions.

Stallergenes has implemented a development plan in order to make available to patients an immunotherapy tablet to treat allergic rhinitis from house dust mites, currently in phase III in Europe. In Japan, clinical development, led by our partner Shionogi, continues as scheduled. A phase IV/III clinical study is in progress. In the United States, a phase III clinical study is being prepared.

Key figures

House dust mites are the LEADING CAUSE of allergic rhinitis worldwide (13).

51% (4) of allergic patients in Europe and the United States and
57% (8) in Japan suffer from allergic rhinitis caused by house dust mites.

1 Tonne of house dust mites produced each year by Stallergenes, which corresponds to breeding 90 billion house dust mites every year.

Nearly 1,500 patients involved in Stallergenes’ house dust mite clinical studies.
“I think that most people don’t realise how painful it can be. When you don’t have an allergy, you have no idea what it is like.” (Sébastien, 33)

“Throughout your life, you have to be scrupulous in terms of cleanliness, follow a course of treatment, take care when you don’t sleep at home, etc. You experience constraints every day.” (Francisco, 53)

“An allergic attack makes you tired and stressed, you get irritated more easily.” (Romain, 33 ans)

“Even at work it has consequences: I couldn’t work at the same level as my colleagues due to tiredness and difficulties in concentration caused by it. Imagine having a bad cold for weeks: as the days go by you feel more and more tired. It’s very unpleasant.” (Nuria, 42)

“As I suffer from a house dust mite allergy, I don’t start any activity without thinking about the effect it will have on my allergy.” (Carmen, 56)

“My friends and family think I am always ill and always complaining.” (José-Luis, 30)

The Environmental Exposure Chamber enables participants to be exposed to selected allergens whose level and variability are controlled.

The VO67.10 clinical study of 355 adult patients allergic to house dust mites aimed to assess the efficacy and tolerance of a 6-month treatment course of immunotherapy tablets.

This study could represent a major advance in the development of our sublingual house dust mite immunotherapy tablets.
Stallergenes invests approximately 20% of its annual revenue in Research & Development. Over the last 5 years, the cumulative investment reached €200 million. This commitment to innovation enables the continued development of immunotherapy tablets which will meet the needs of 80% of respiratory allergy cases: as well as Oralair® and the house dust mite tablet, three other pharmaceutical specialties related to the treatment of allergic rhinitis for birch, Cryptomeria Japonica (commonly known as Japanese cedar) and ragweed pollens are in development. In asthma treatment, the programme is producing initial conclusive results.

UNMET THERAPEUTIC NEEDS IN THE TREATMENT OF ASTHMA

2.7 million, or half of asthmatic patients undergoing treatment suffer from uncontrolled asthma, spread evenly over Europe and the United States.

None of the treatments currently available have demonstrated a lasting effect. Convinced of the strong potential of sublingual immunotherapy to treat this debilitating disease, in 2012 Stallergenes carried out a phase I study of asthma caused by house dust mites, Stallergenes is very much focused on innovation and has based its development on its knowledge of allergens, which underpins its core expertise. Having established a deep understanding of personalised medicine, today the Group is developing pharmaceutical specialties.

INNOVATION, A FUTURE GROWTH DRIVER

Interview with
Professor Stephen T. Holgate, Medical Research Council (MRC) Clinical Professor of Immunopharmacology at the Faculty of Medicine, Southampton, United Kingdom.

What are the unmet therapeutic needs in the treatment of asthma?

Every asthma patient is different, whilst recommendations are designed for a homogenous population. Applying recommendations depends on the severity of the condition, whereas its cause deserves more attention. In addition, certain asthma patients do not like inhaling medication on a regular basis, which can cause them not to take medication correctly. This is especially true in the case of young people.

How can immunotherapy meet these needs?

Allergen immunotherapy is having an effect on the allergy march, especially for children, for whom sublingual immunotherapy is a practical and easily tolerated option. It has shown great efficacy in allergic conditions of the upper respiratory tract. As these illnesses are linked to those affecting the lower respiratory tract, there is a real opportunity to redesign immunological responses to consider, for asthma treatment, targeted and layered medication, based on the cause of the illness. Initial data is very encouraging but has yet to be consolidated. Improving the scientific justification will allow to demonstrate that allergen immunotherapy can be a major therapeutic option in the treatment of allergic asthma.

AIT is a promising option for asthma treatment.
with results providing positive tolerance data in comparison with high dosage treatments, and has just launched a phase II clinical study.

IMMUNOTHERAPY BOOSTS EFFICACY OF BIRCH POLLEN ALLERGY TREATMENTS

Birch pollen allergy affects 27% of allergy sufferers in Europe and 28% in the United States and causes sudden and intense attacks. Stallergenes conducted a clinical study (VO68.10) in Europe on Staloral® Birch, a solution-based treatment. Staloral® showed significant efficacy against rhin Conjunctivitis in this, the largest ever study of sublingual immunotherapy for birch pollen carried out to date. The efficacy of treatment increased between the first pollen season and the second, providing results that are promising for the future.

IN JAPAN, ADDRESSING A PUBLIC HEALTH ISSUE

The Cryptomeria Japonica pollen immunotherapy tablet is currently under clinical development, led by our Japanese partner Shionogi, one of the leading Japanese pharmaceutical companies. The product is soon to enter into phase I.

RESEARCH PROJECTS FOR MORE EFFECTIVE TREATMENTS

Stallergenes is currently working on immune responses as well as on identifying biomarkers, biological parameters whose qualitative or quantitative variation allows for a predicted clinical response to treatment. The Group is seeking to develop second-generation allergen immunotherapy products, thanks to the use of formulation and additives, which can be combined with recombinant allergens.

Continued investment in innovative technologies

Emmanuel Nony, Head of Characterisation and Proteomics, Pharmaceutical Research & Development at Stallergenes

When developing a new allergen immunotherapy product, it is essential to characterise and quantify the allergens present in a candidate drug. The use of mass spectrometry allows us to identify the best candidates for further development of a new product by checking for the presence of the major allergens which must be present in the products. We also use this cutting-edge technology in the development of production processes by monitoring the quality of raw materials and by checking the integrity and exact amount of allergens present in the pharmaceutical product, in order to ensure their conformity.
01

Grass pollen extracts, corresponding to the epidemiological characteristics that patients are exposed to, are used in the production of Oralair®. Each species pollinates for between 1 and 3 weeks of the year. Harvesting must be carried out during this very short period.

02

Stallergenes has designed harvesting machines, specially adapted for collecting pollen from the plant by suction, ensuring a very pure quality of pollen is obtained. The design of these machines, which use technology unique anywhere in the world, is covered by three patents.

03

Stallergenes has entered into a close and unprecedented collaboration with grain farmers in the Centre of France region. Today, grass production covers nearly 100 hectares. Its operation is subject to strict guidelines, banning the use of pesticides and chemical fertilisers.

OPEN FIELD FOR GRASSES

Stallergenes is the leading global pharmaceutical producer of house dust mites and grass pollens.

Integrating production of the main raw materials allows strategic challenges to be addressed with the aim of improving:
- the controlling of supplies
- the industrial process
- quality control
04
After harvesting, the pollen goes through an initial crushing stage.

05
After crushing come stages involving sifting, drying and storing the raw material.

06
Every stage of production is subject to rigorous checks. The production facility combines both agronomic and biopharmaceutical expertise.

07
The raw material undergoes successive stages of conversion in compliance with Good Manufacturing Practice, prior to purified pollen being obtained. With its raw material facility, Stallergenes aims to meet more than 50% of its grass pollen requirements.
Stallergenes has developed a specific culture medium, Stalmite APF® (Animal Protein Free), which relies on a feeding standard for house dust mites free of animal and human proteins, based on amino acids and plant based extracts, in optimal temperature and humidity conditions.
03

House dust mites are fed 3 times during breeding, in amounts adapted to each species.

04

Growth in breeding is monitored daily (population, activity, density). Several critical parameters are studied, depending on each species: humidity, temperature, food, periodical movement to avoid moisture concentration.

05

Production is monitored internally from the raw material through to the finished product, and is subject to rigorous checks at every stage so that patients are supplied with pharmaceutical grade products.

06

Every stage of the process is standardised in order to ensure optimal growth and reliable batch-to-batch consistency.
An evolving company, Stallergenes has quadrupled in size in ten years. In order to support our growth, we have doubled our workforce in six years, with the aim of becoming a global player. Over the last few years, we have strengthened our organisation in both the scientific domain and in international operations. The structure is guided by improving performance, supported by human resource indicators and a proactive salary policy.

**AN INCREASINGLY INTERNATIONAL STRUCTURE**

Stallergenes’ growth is driven by its international business. The Group has doubled its number of subsidiaries in recent years and now has 18 affiliates worldwide. This international expansion has enabled the company to consolidate the workforce at its head office with people from other backgrounds, guaranteeing a wealth of experience and an open mind, and it has helped our affiliates to find suitable candidates. More than 30 nationalities are today represented within the company.

To ensure the link between affiliates and head office, we have drawn on a pool of young, internationally mobile talents. The arrival of new nationalities at all levels of the Company has led us to develop a new managerial culture and to reflect upon our values.

**A company mind-set captured in four values**

**Empowerment:** As responsible people within our field of expertise, we have the necessary autonomy to make decisions that will enable us to achieve our objectives.

**People:** We are committed to enabling each of our employees to achieve his / her full potential, be it individually or collectivly, in an environment of mutual respect and trust.

**Entrepreneurship:** Our vision is to innovate, create and successfully complete projects with determination and by taking ownership of them.

**Performance:** To be results and performance oriented by promoting a culture of completing work on time and within budget, with rigour and integrity.
KEY VALUES THAT GUIDE OUR DAY-TO-DAY WORK
Expressing and sharing our common values and our unique know-how are essential elements that enable Stallergenes to attain its objectives. Based on a questionnaire addressed to all employees, followed by an Executive Committee collaborative project, four key values have been identified that reflect a strong company mind-set committed to excellence. The human factor is vital, it is also one of the key features of Stallergenes’ corporate social responsibility.

More than 1,000 employees including 200 in Research and Development

60% of profits reinvested, 40% shared equally between employees and shareholders

CORPORATE RESPONSIBILITY, SHARED BY EVERYONE
A leader in allergen immunotherapy, Stallergenes has set itself the objective, alongside healthcare professionals, to increase the treatment of allergies and to improve the long-term quality of life of sufferers. This commitment forms part of a corporate responsibility policy, which, over and above the conservation of the environment and corporate ethics, is largely focused on patients and employees.

Stallergenes: A committed and responsible company
Patients: Stallergenes is dedicated to Research in the service of its patients, which results in the development of innovative therapeutic solutions, using tailored protocols, and by supporting both specialist physicians and patients.

Employees: The Group enables its employees to adapt to an evolving pharmaceutical environment and values their commitment by ensuring that profits are distributed fairly: 40% are shared equally between employees and shareholders, with the remaining 60% reinvested in the business.

Ethics and governance: Mindful of providing high quality information to physicians and patients, Stallergenes supports the leading international stakeholders in allergology. The Group has a balanced governance structure and benefits from a stable shareholding.

Environnement: Following its 2010 initiative to carry out a first carbon footprint assessment, the Company introduced measures to increase employee responsibility for reducing their environmental footprint: eco-driving, car sharing, waste sorting, etc.

We’re Fighting the Same Fight
I Have a Severe Respiratory Allergy
I’m an Immunotherapy Researcher

The commitment forms part of a corporate responsibility policy, which, over and above the conservation of the environment and corporate ethics, is largely focused on patients and employees.
Balance sheet at 31 December 2012

<table>
<thead>
<tr>
<th>(€ millions)</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Goodwill</td>
<td>28.3</td>
<td>33.4</td>
<td>33.7</td>
<td>33.4</td>
<td>33.3</td>
</tr>
<tr>
<td>Land and building</td>
<td>17.4</td>
<td>16.8</td>
<td>16.2</td>
<td>21.0</td>
<td>23.0</td>
</tr>
<tr>
<td>Other non-current assets, net</td>
<td>31.6</td>
<td>34.7</td>
<td>41.5</td>
<td>44.7</td>
<td>44.0</td>
</tr>
<tr>
<td>Operating working capital requirements</td>
<td>14.9</td>
<td>12.9</td>
<td>2.8</td>
<td>4.7</td>
<td>11.0</td>
</tr>
<tr>
<td>Cash and cash equivalents</td>
<td>8.6</td>
<td>21.8</td>
<td>67.1</td>
<td>77.0</td>
<td>95.8</td>
</tr>
<tr>
<td><strong>TOTAL ASSETS</strong></td>
<td><strong>100.8</strong></td>
<td><strong>119.6</strong></td>
<td><strong>161.3</strong></td>
<td><strong>180.9</strong></td>
<td><strong>207.1</strong></td>
</tr>
<tr>
<td>Shareholders’ equity</td>
<td>82.6</td>
<td>102.7</td>
<td>131.2</td>
<td>159.6</td>
<td>188.8</td>
</tr>
<tr>
<td>Property loans</td>
<td>11.2</td>
<td>9.9</td>
<td>8.5</td>
<td>7.0</td>
<td>5.4</td>
</tr>
<tr>
<td>Other borrowings</td>
<td>7.0</td>
<td>7.0</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Deferred income from partnerships</td>
<td>-</td>
<td>-</td>
<td>21.6</td>
<td>14.3</td>
<td>12.9</td>
</tr>
<tr>
<td><strong>TOTAL EQUITY AND LIABILITIES</strong></td>
<td><strong>100.8</strong></td>
<td><strong>119.6</strong></td>
<td><strong>161.3</strong></td>
<td><strong>180.9</strong></td>
<td><strong>207.1</strong></td>
</tr>
</tbody>
</table>

Our EBITDA has doubled since 2008. In 2012, we increased the net cash position by €20 million. It currently stands at €90 million.
Income statement and cash flows

<table>
<thead>
<tr>
<th>(€ millions)</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sales</td>
<td>168.9</td>
<td>190.6</td>
<td>213.8</td>
<td>232.3</td>
<td>239.8</td>
</tr>
<tr>
<td>Cost of goods sold</td>
<td>(28.7)</td>
<td>(32.1)</td>
<td>(37.4)</td>
<td>(43.8)</td>
<td>(46.3)</td>
</tr>
<tr>
<td>Selling, general and admin. expenses</td>
<td>(82.1)</td>
<td>(87.7)</td>
<td>(99.6)</td>
<td>(108.5)</td>
<td>(114.2)</td>
</tr>
<tr>
<td>Research and development costs</td>
<td>(36.6)</td>
<td>(46.2)</td>
<td>(41.2)</td>
<td>(41.6)</td>
<td>(38.6)</td>
</tr>
<tr>
<td>R&amp;D-related income</td>
<td>6.6</td>
<td>7.6</td>
<td>9.7</td>
<td>16.2</td>
<td>14.9</td>
</tr>
<tr>
<td><strong>Operating profit (EBIT)</strong></td>
<td>28.1</td>
<td>32.2</td>
<td>45.3</td>
<td>54.6</td>
<td>55.6</td>
</tr>
<tr>
<td>Non cash items</td>
<td>6.2</td>
<td>7.5</td>
<td>11.0</td>
<td>9.7</td>
<td>13.7</td>
</tr>
<tr>
<td><strong>Gross operating profit (EBITDA)</strong></td>
<td>34.3</td>
<td>39.7</td>
<td>56.3</td>
<td>64.3</td>
<td>69.3</td>
</tr>
<tr>
<td>Current income tax on operating activities</td>
<td>(7.8)</td>
<td>(8.4)</td>
<td>(14.4)</td>
<td>(17.8)</td>
<td>(19.1)</td>
</tr>
<tr>
<td>Change in working capital requirements</td>
<td>(3.5)</td>
<td>2.2</td>
<td>10.1</td>
<td>(1.9)</td>
<td>(6.3)</td>
</tr>
<tr>
<td>Capital expenditure</td>
<td>(18.3)</td>
<td>(16.0)</td>
<td>(16.7)</td>
<td>(17.4)</td>
<td>(13.8)</td>
</tr>
<tr>
<td>Advanced payments from partnerships</td>
<td>-</td>
<td>-</td>
<td>21.6</td>
<td>(7.3)</td>
<td>(1.4)</td>
</tr>
<tr>
<td><strong>Free cash flow</strong></td>
<td>4.7</td>
<td>17.5</td>
<td>56.9</td>
<td>19.9</td>
<td>28.7</td>
</tr>
<tr>
<td>Dividends</td>
<td>(5.2)</td>
<td>(5.9)</td>
<td>(7.3)</td>
<td>(10.1)</td>
<td>(10.1)</td>
</tr>
<tr>
<td>Share transactions</td>
<td>1.7</td>
<td>3.2</td>
<td>4.1</td>
<td>1.4</td>
<td>1.1</td>
</tr>
<tr>
<td>Cost of net financial debt and other</td>
<td>(0.4)</td>
<td>(0.4)</td>
<td>(0.2)</td>
<td>0.1</td>
<td>0.7</td>
</tr>
<tr>
<td><strong>Change in net financial debt</strong></td>
<td>0.8</td>
<td>14.4</td>
<td>53.5</td>
<td>11.3</td>
<td>20.4</td>
</tr>
</tbody>
</table>

Stock market data

<table>
<thead>
<tr>
<th></th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average diluted number of shares (millions)</td>
<td>13.31</td>
<td>13.36</td>
<td>13.46</td>
<td>13.52</td>
<td>13.54</td>
</tr>
<tr>
<td>Average share price (€)</td>
<td>46.76</td>
<td>48.17</td>
<td>58.13</td>
<td>51.82</td>
<td>43.97</td>
</tr>
<tr>
<td>Market capitalisation (€ millions)</td>
<td>622</td>
<td>644</td>
<td>783</td>
<td>701</td>
<td>595</td>
</tr>
<tr>
<td>Earnings per share, net. diluted (€)</td>
<td>1.43</td>
<td>1.66</td>
<td>2.29</td>
<td>2.73</td>
<td>2.76</td>
</tr>
<tr>
<td>Average PER</td>
<td>31.8</td>
<td>29.0</td>
<td>25.4</td>
<td>19.0</td>
<td>15.9</td>
</tr>
</tbody>
</table>

Stock market performance

The following analyst firms track the Group’s share: CM-CIC, Gilbert Dupont, Exane BNP Paribas, ID midcaps, Kepler Cheuvreux, Natixis, Oddo, Portzamparc, SG securities, Standard & Poor’s.

All our financial information is available on http://finance.stallergenes.com
GLOSSARY

Conditions

• **Allergic rhinitis**: an illness characterised by inflammation of the nasal mucosa which can cause a range of symptoms: runny nose, blocked nose, sneezing fits, itchy nose and/or palate. These symptoms are often accompanied by conjunctivitis, which manifests itself by lacrimation, a tingling sensation, red eyes and a poorer sense of smell.

• **Allergic asthma**: infection caused by inflammation of the airways, associated with a hyperactivity of the bronchus. An asthmatic episode can rapidly bring on sudden asphyxia with a lack of oxygen, wheezing in the chest, dyspnoea and anxiety.

Treatments

• **Allergen Immunotherapy (AIT)**: medical treatment aimed at treating allergic pathologies, enabling the immune system to be re-educated. Increasing doses of allergens are administered to re-acustom the body to substances that are generally harmless (pollens, house dust mites), thereby leading to long-term tolerance. By repeatedly exposing patients to the allergen responsible for their symptoms, the physician aims to achieve short-term relief as early as in the first year, meaning that their patients no longer suffer in their daily lives. The medium term goal, after three years of treatment, is to maintain this effect in the years after treatment ends through “desensitisation”. Allergen immunotherapy may be administered under the tongue (sublingual) in drop or tablet form, or by injections under the skin (subcutaneous).

Notes

(1) Datamonitor Allergic Rhinitis 2010
(2) Health at a Glance Europe 2012, by OECD
(3) Nathan et al., 1997
(4) Arbes et al., 2005
(5) Salo et al., 2011 for Birch
(6) Bauchau et al., 2004
(7) Bousquet et al., 2007. For countries not mentioned in the paper, the most similar country climate has been retained as a reference for sensitization rate – Stallergenes internal estimations
(8) Sakashita et al., 2010
(10) Yu Minami et al., 2010: Japanese cedar pollinosis impact on work productivity, quality of life, and symptoms 2008 vs. 2009
(11) Stallergenes Internal Estimate
(12) Allergy Asthma Information Association / L-P Boulet et al., Clinical and Experimental Allergy 1997, volume 27, pages 52-59
(13) USA: Arbes et al., 2005; Europe: Bousquet et al., 2007, for countries not mentioned in the paper, the most similar country climate has been retained as a reference for sensitization rate: Japan: Sakashita et al., 2010
(16) ISAC Lancet 2008
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