



life *beyond* allergy

STALLERGENES  GREER™

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Stefan Meister

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Michele Antonelli



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“Stallergenes Greer is delivering in the short-term while building for the long-term.”

Stefan Meister

chairman's message

Stefan Meister *Chairman of the Board of Directors*

Looking back on 2021, we can be proud of the way Stallergenes Greer navigated successfully through times of disruption and change, still marked by the global pandemic, while continuing to serve patients and healthcare professionals with excellence. The Group remained steadfast in its ambition to become the world's leading allergen immunotherapy company by executing its strategy with discipline and determination.

For a second consecutive year, Stallergenes Greer posted record performance, delivering beyond objectives. The Group's significant achievements include: substantial market share gains, a strengthened presence in the European market with the launch of our allergen immunotherapy tablet and new allergen references, as well as dynamic sales in the U.S. veterinary allergy market.

This performance is essential in maintaining Stallergenes Greer's financial strength and in continuing to transform the Group for the future. Throughout the year, we continued to invest in our manufacturing capabilities while bolstering R&D efforts, both internally and externally via a series of long-term collaborations with academic and private partners who are at the cutting edge of scientific innovation.

With robust results, smart capital allocation and the support of B-FLEXION (formerly Waypoint Capital), its sole shareholder, Stallergenes Greer is delivering in the short-term while building for the long-term. The Group is exploring new growth horizons; notably: novel drug delivery technologies; expansion into the food allergy market; highly targeted acquisition opportunities; and, growing its geographic footprint.

On behalf of the Board of Directors, I would like to take this opportunity to recognise the contribution of Stallergenes Greer's employees to the Group's success and thank them for their unwavering commitment to delivering on our promise to patients and the medical community.

We can look ahead with confidence. In the future, Stallergenes Greer will continue to capitalise on its century of experience in allergen immunotherapy while accelerating innovation and growth for the benefit of all its stakeholders.

Sincerely,

Stefan Meister

interview with *our CEO*

Michele Antonelli *Chief Executive Officer*

What did Stallergenes Greer accomplish in 2021 and how is the Group delivering on its strategy?

In a context still marked by the pandemic and despite increased competition, Stallergenes Greer posted record performance, with double digit growth in many countries. We consolidated our leadership positions in the U.S., France, Italy, Spain, the Czech Republic, Australia and Russia, while continuing to grow market share in a number of other geographies. This success also reflects Stallergenes Greer's ability to maintain product delivery thanks to a state-of-the-art supply chain with a zero back order target.

The launch of Orylmyte®, our house dust mite sublingual allergen immunotherapy tablet, in Germany, Belgium and Luxembourg was also a significant success, with results above our expectations. The performance of Orylmyte® in the German market – a country in which patients and the medical community are rapidly adopting SLIT treatment solutions – is an important indicator of the appreciation our tablet should also receive when launched in other European countries during 2022 and 2023.

From an operational standpoint, we achieved significant efficiencies which allow us to allocate additional resources to industrial upgrades, innovation in novel delivery technologies and life-cycle management, as well other strategic initiatives.

These solid performances reflect the value proposition of Stallergenes Greer: a high-quality product portfolio, a commitment towards our stakeholders and the engagement of our employees towards improving quality of life for people with allergies, by leveraging the potential of precision medicine.

What role has Stallergenes Greer's cultural transformation played in this success?

Stallergenes Greer has definitively shifted into a culture of performance. The strategy is translated into long- and short-term objectives and hence into projects. Our project management organisation is developing new project leaders and each initiative is constantly monitored to achieve effective progress. Our ways of working ensure agility and the proper use of resources.

This performance-oriented organisation has not only improved the recognition of how employees contribute to the success of the Group but has also given rise to an energetic and positive mindset shared at all levels of Stallergenes Greer.

Our mission is to better serve our patients and the medical community. And, by focusing our efforts on what is essential for Stallergenes Greer, by being clear about our objectives, by learning to swiftly adapt to change, we are accomplishing our mission with pride, confidence and renewed vigour.

What do you believe are the most important drivers for growth going forward?

Stallergenes Greer's primary growth drivers will stem from innovation through the expansion of our allergen immunotherapy offering in the field of food allergies, and through investments in the development of new biotechnologies for novel drug delivery. For example, we are currently investigating and evaluating modern vector-based delivery technologies, such as messenger RNA.

The success of our SLIT technologies will also play an important role as we continue to develop our Orylmyte®/ Actair® and Oralair® tablets, alongside our existing sublingual drop treatment, Staloral®. The amplification of our presence in larger markets, such as China, will also have a positive impact on Stallergenes Greer's growth.

How is precision medicine shaping the future of allergy care?

Precision medicine is fundamental to the future of allergy care.

The development of targeted approaches to patient profiles or the characterisation of specific epitopes, will not only improve disease outcomes for patients but also contribute to a better understanding of both the mechanism of disease and the immunological system response.

Discoveries in precision medicine will inspire the scientific community to consider allergy as a field in which additional knowledge can be generated; knowledge which, in turn, should rapidly deliver new solutions for people with allergic diseases. With the increasing prevalence of allergic diseases and the significant impact of environmental pollution on human health, discoveries based on precision medicine will play a fundamental role in the future of our industry. Stallergenes Greer has historic experience in clinical trials in the AIT space and initiated the development of real world evidence in the field of allergy. Very large population data provide new evidence of the efficacy of our treatments in real life, notably a significant reduction of incumbent disease. Our medical teams continue to



successfully build on real-world evidence to further allergen immunotherapy.

How does Stallergenes Greer create a sustainable future for its stakeholders?

In a world affected by climate change, environmental pollution and urbanisation, more and more people are affected by allergies and, globally, among school children sensitisation rates to one or more common allergens, including food, are currently approaching 40%-50%¹. The molecular structure of certain allergens can adapt to environmental change and their allergenic potential is increasing. We all have a part to play in the fight against climate change to contribute to building a sustainable future for all.

Stallergenes Greer promotes environmentally conscious behaviours throughout the Group, thus ensuring a safe work environment for our employees and partners. As part of the Group's corporate responsibility strategy, we are currently reassessing our environmental impact.

Since its delisting in 2019, Stallergenes Greer's management focused on operational excellence. Our objectives have been reached and with the sustained support of our shareholder, we are now in a position to broaden our outlook to the 2030 horizon, in particular with regard to the development of a robust pipeline based on novel technologies and precision medicine, the expansion of our geographic footprint and a presence in the field of food allergies.

I am confident in our future, in our people and in our ability to break new ground in the treatment of allergic diseases thanks to our expertise in biotechnology, our commitment to innovation, our engagement towards patients and the medical community and our pioneering spirit.

1. World Health Organization. *White Book on Allergy 2011-2012 Executive Summary*. By Prof. Ruby Pawankar, MD, PhD, Prof. Giorgio Walter Canonica, MD, Prof. Stephen T. Holgate, BSc, MD, DSc, FMed Sci and Prof. Richard F. Lockey, MD



Profile



Highlights

2021

FEBRUARY

Stallergenes Greer rolls out new visual guidelines to better reflect the Group's purpose, "enabling precision medicine to improve life for people with allergies", and its long-standing expertise in the development of personalised precision allergen immunotherapy treatments tailored to the individual needs and profile of each patient.

MAY

Positive outcome of the European decentralised registration procedure for the Group's sublingual house dust mite allergen immunotherapy (AIT) tablet. The Paul Ehrlich Institut (PEI), Germany, acted as reference member state on behalf of 21 European countries.

JUNE

Alustal®, the Group's subcutaneous allergen immunotherapy treatment (SCIT) is again available in Spain and Italy following the full resumption of SCIT production in Antony (France).

JULY

Stallergenes Greer showcases its advancements in precision medicine in AIT at the EAACI 2021 Congress via a company-sponsored symposium and the presentation of nine posters addressing precision medicine in AIT and revealing new data from clinical trials and real-world studies.

Stallergenes Greer and Alyatec, a contract research organisation based in Strasbourg University Hospital (France), announce a research collaboration to advance precision medicine in AIT. With this collaboration, Stallergenes Greer aims to strengthen its precision medicine-based approach and the management of patients with allergies by expanding its knowledge of allergy pathophysiology and endotypes, AIT mode of action and clinical validation.

SEPTEMBER

Germany is the first European country to launch Stallergenes Greer's house dust mite AIT tablet marketed under the brand name Orylmyte®. With this newly registered product, the Group further strengthens its sublingual offering in the German market.

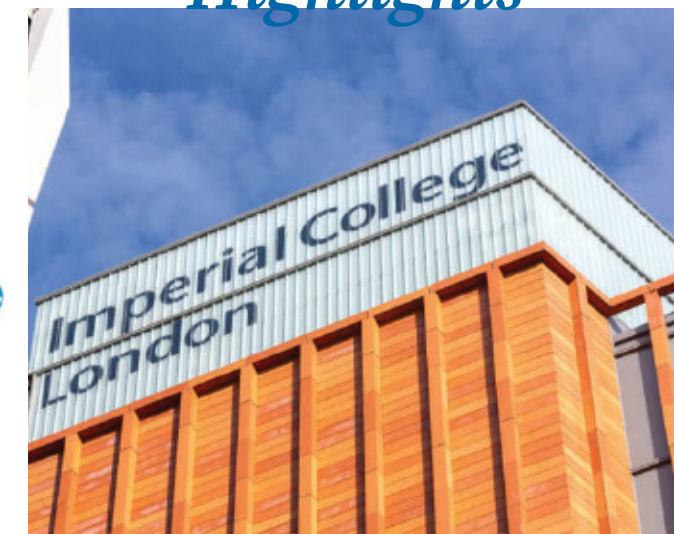
Stallergenes Greer holds a major scientific standalone congress in Berlin (Germany). The congress, entitled "New Era in AIT: Offering Personalised and Precision Medicine", brought together on site 188 key external experts, allergy specialists and healthcare professionals from 15 countries.

OCTOBER

Stallergenes Greer launches Orylmyte® in Luxembourg.

Stallergenes Greer enters into an exclusive partnership with Aptar Pharma, a global leader in drug delivery systems, services and active material science solutions, for the development of the first of its kind connected device and companion mobile app for patients undergoing Stallergenes Greer's AIT treatments with sublingual solutions.

Stallergenes Greer launches CORAP (Community for Research in Allergic Patients), a programme which notably includes a research plan aiming to provide additional knowledge about the various types of respiratory allergies via clinical projects and evaluate the impact of allergen immunotherapy on the quality of life of patients and other relevant patient reported outcomes. Patients undergoing Stallergenes Greer's AIT treatments can join the CORAP community, on a voluntary basis, and thus participate in the various stages of the Group's research initiatives.



2022

NOVEMBER

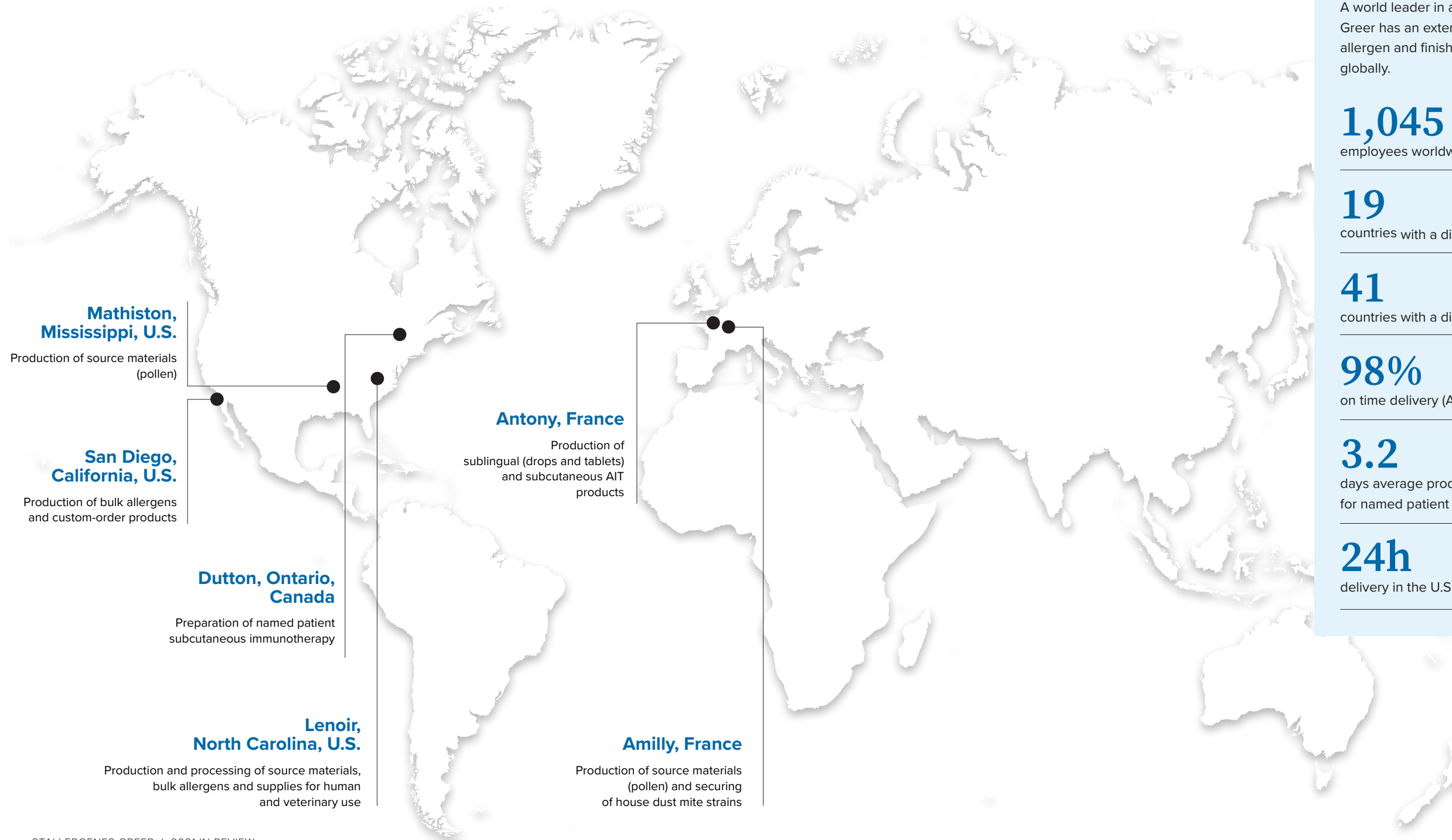
Stallergenes Greer launches Orylmyte® in Belgium

JANUARY

Stallergenes Greer enters into a research collaboration with Imperial College London, a pioneer and world-leading university in the biomarker field. The long-term research collaboration focuses on the identification of biomarkers of AIT efficacy and aims to expand knowledge regarding the pathophysiology of allergic diseases and their treatment with AIT.

Stallergenes Greer is a fully integrated global biopharmaceutical company specialising in the diagnosis and treatment of allergies through the development and commercialisation of allergen immunotherapy (AIT) products and services.

The Group's extensive product portfolio, available in multiple formulations (subcutaneous, sublingual drops and tablets), offers patients innovative solutions to improve quality of life for people with allergies.



A world leader in allergen immunotherapy, Stallergenes Greer has an extensive global footprint and the largest allergen and finished AIT product manufacturing capacity globally.

1,045
employees worldwide

19
countries with a direct presence

41
countries with a distribution network

98%
on time delivery (Antony manufacturing plant)

3.2
days average product lead time packaging in Antony for named patient products

24h
delivery in the U.S.

Stallergenes Greer is a purpose-driven, ambition-led company. We operate to improve life for people with allergies and deliver sustained growth to create value for all our stakeholders.

Our purpose

Enabling precision medicine to improve life for people with allergies.

Our extensive portfolio of allergens and drug delivery modes provide physicians with the flexibility to adapt treatments to the individual characteristics and mechanism of disease of each patient

Our ambition

Becoming the world's leading allergen immunotherapy company.

By:

- realising the potential of precision medicine combined with personalised healthcare to improve the quality of life of people with allergies,
- changing the course of allergic disease through the largest portfolio of best-in-class allergen immunotherapy (AIT) treatments,
- remaining a trusted partner in allergy management and making a lasting and positive contribution to society,
- nurturing scientific innovation and collaboration to deliver sustained growth and value creation for all our stakeholders,
- ensuring continuous improvement in operations to provide the right product to the right patient on time, every time.



Our strategy

Stallergenes Greer is delivering on its strategy by leveraging its strengths, developing its expertise and encouraging innovation to generate sustainable growth.

Precision medicine for better patient care

Stallergenes Greer is committed to furthering precision medicine and personalised AIT treatments to improve life for people with allergies.

We develop diagnostic tools and AIT treatments which allow to both identify the patients most likely to benefit significantly from AIT and to choose the appropriate treatment for them.

Our extensive product portfolio spanning all delivery modes (subcutaneous and sublingual), and precise personalised treatment solutions provide unparalleled patient care tailored to the needs of both individual patient profiles and the medical community.

Investing in our people

Stallergenes Greer is driven by an entrepreneurial mindset. We believe there are no limits to what we can do as a team.

We invest in our people and create a learning culture so we can all reach our potential, together.

Our patients are at the heart of every decision we make and inspire us to always go further.

We are committed to building world-class competencies in science, supply and quality. Our employees are empowered to effect positive change.

A high-performance agile business model

Stallergenes Greer is a resource-efficient organisation. Our lean operating model focuses on quality and robust operations.

We build on our strong foundations to seize profitable growth opportunities by developing new business in additional geographies and markets, and through external growth by seeking to add new expertise and innovation both in our core business and in related therapeutic areas.

Executive committee

Stallergenes Greer is governed by a Board of Directors which determines the strategic direction of the Group.

The Executive Committee, chaired by the Chief Executive Officer, is comprised of senior leaders from across the Group who represent a breadth and depth of knowledge and experience to lead our business. Together, they form a forward-thinking, collaborative, multicultural group of leaders that drive our culture of success and support our growth worldwide.

Michele Antonelli

Chief Executive Officer

Michele Antonelli has been CEO of Stallergenes Greer since January 2019. He joined the company in 2015 as Head of Europe and International. Previously, Michele Antonelli held roles of increasing responsibility and scope at UCB, most recently serving as EVP and Head of Immunology Europe, overseeing the region's commercial, medical, and market access activities. Prior to UCB, Michele Antonelli spent 16 years at Merck Serono, ultimately serving as SVP and Global Head of Biotech Manufacturing and Process Development. Michele Antonelli is Swiss and Italian.

Valérie Benhamou

General Counsel

Valérie Benhamou joined Stallergenes Greer in 2017 as Associate General Counsel Europe and International. Valérie Benhamou joined the company from Abbott, where she was Senior Legal Counsel for France, Benelux and Africa. Prior to Abbott, she served as Senior counsel for Bristol-Myers Squibb where she provided legal support to all divisions in France and to EMEA commercial operations and practiced at law firms where she focused on healthcare matters. She has been a member of the Paris Bar since 1999. Valérie Benhamou is French.

Amer Jaber

Executive Vice President Operations, Europe and International

Amer Jaber joined Stallergenes Greer in 2018. Prior to joining Stallergenes Greer, Amer Jaber was Head of Biotechnology Operations at R-Pharm responsible for developing the long-term strategy and execution of technical operations for CMC Development and Manufacturing. Amer Jaber was previously Head of Global Biotech Development and Manufacturing for Technical Operations and Managing Director of UCB Switzerland. Before joining UCB, he held roles of increasing responsibility at Mondobiotec, Serono International and Rivopharm. Amer Jaber is Lebanese and Swiss.

Nicola Lamacchia

Chief Financial Officer

Nicola Lamacchia joined Stallergenes Greer in 2017 as Head of Finance for the Europe and International region. Prior to joining Stallergenes Greer, he was Head of Finance for International at Shire, leading the creation of a new financial framework and supporting the company's growth and expansion. Prior to Shire, Nicola Lamacchia held several country, regional and division-level financial roles at Merck Serono. Nicola Lamacchia is Swiss and Italian.

Tibor Nemes

Executive Vice President, Head of Americas

Tibor Nemes joined Stallergenes Greer in 2016 and served as Global Head of Technical Operations before taking over as Head of the Americas in May 2018. Tibor Nemes previously spent eight years at Novartis where he held roles of increasing responsibility, most recently as the Global Operations Head, Tech Ops Manufacturing, Strategy and BDM&A. Prior to Novartis, Tibor Nemes held Engineering and Operations leadership roles at Novavax, Inc., Bristol-Myers Squibb Company, Elan Pharmaceuticals and Hypex, Inc. Tibor Nemes is American.

Dominique Pezziardi

General Manager France, Belgium and Luxembourg - Global Head of Pricing and Market Access

Dominique Pezziardi joined Stallergenes Greer in 2012 as Head of Strategy and Business Operations. Prior to joining Stallergenes Greer, Dominique Pezziardi gained his expertise in several therapeutic fields including fertility, growth hormones, diabetes, rare diseases, cardiology and medical devices in the pharmaceutical sector at Ciba, Sanofi and Merck Serono. He successfully managed global product launches, life cycle development plans, mature franchise relaunches, alliances with strategic partners, and more recently, corporate strategy development. Dominique Pezziardi is French.

Jérôme Tilly

Senior Vice President, People Operations

Jérôme joined Stallergenes Greer in 2014 as Senior Vice President Human Resources, Europe and International. Jérôme Tilly joined the company from Sogefi, an Italian automotive supplier, where he served as Vice President Human Resources. Throughout his career, Jérôme held positions of increasing responsibility and gained in-depth knowledge of human resources at automotive, airport ground handling and media companies. Jérôme Tilly is French.

Petr Tor

Senior Vice President, Commercial Operations, Europe and International

Petr Tor joined Stallergenes Greer in 2010 as General Manager of the Czech and Slovak subsidiary and since 2014 he has held commercial responsibilities for various regions of increasing scope and complexity in Europe, the Middle East and Africa. Petr Tor gained his expertise in several therapeutic fields including asthma, cardiology, diabetes, glaucoma, antibiotics and HIV at Merck & Co., where he spent 16 years. Petr Tor is Czech.



From left to right: Jérôme Tilly, Valérie Benhamou, Amer Jaber, Michele Antonelli, Nicola Lamacchia, Dominique Pezziardi, Petr Tor, Tibor Nemes

Stallergenes Greer is a private company owned by interests associated with the Bertarelli family, which are advised by the B-FLEXION group (formerly Waypoint Capital). B-FLEXION is a private, entrepreneurial investment firm, delivering exceptional value over the generations, while also contributing positively to society.

B-FLEXION continues to drive expansion by growing operating businesses in transformative industries. In keeping with – and building upon – its heritage, these are principally in the fields of life sciences, healthcare services and digital health.

Chaired by Ernesto Bertarelli, B-FLEXION has offices across Europe and in the United States.

Stallergenes Greer's shareholding structure ensures the Group remains fully focused on its purpose, "enabling precision medicine to improve life for people with allergies", and the execution of its business objectives.



The precision
patients deserve

Precision *medicine*

Fulfilling our promise to patients and healthcare professionals

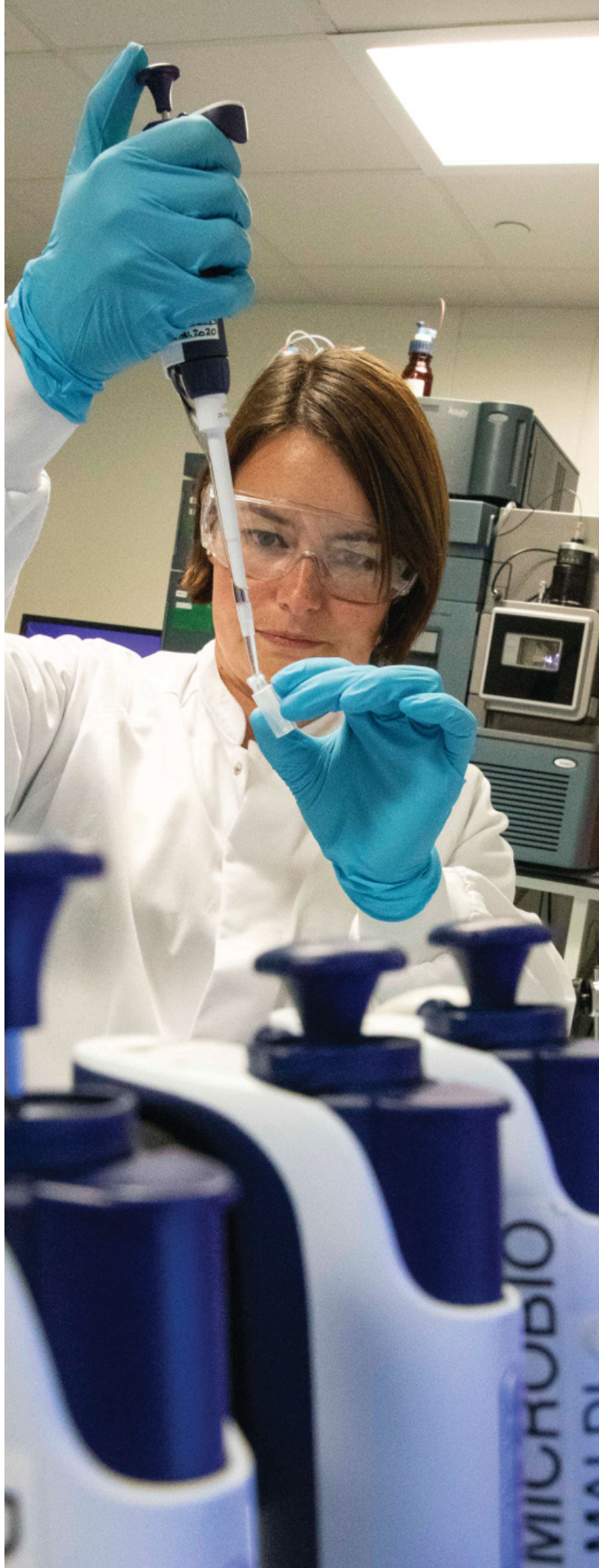
Precision medicine consists in using the individual characteristics and mechanism of disease of each patient to determine which treatment is the most likely to maximise treatment effectiveness, while reducing costs both for patients and healthcare authorities.

At Stallergenes Greer, we believe that patients deserve an allergen immunotherapy solution that is tailored to their needs and profile. We are pushing the boundaries of R&D to fully leverage the potential of precision medicine for the benefit of people with allergies. One of the ways we are doing this is by characterising the molecular immunological responses of each patient and exploring molecular diagnostics to identify, with increased precision, the allergens to which each patient is specifically sensitive.

The development of new disciplines and skills are making it possible to specify the diagnosis of respiratory allergy for each individual. Molecular diagnostics provide additional information to guide the prescription and composition of allergen immunotherapy treatments.

Precise personalised allergen immunotherapy solutions

Because each patient presents a unique immunologic profile, we believe that one solution doesn't fit all. Stallergenes Greer's approach allows healthcare professionals to create, along with first-line treatments such as allergen evicition and symptomatic medication, a tailored approach that best addresses each individual's treatments needs.



Professor Philippe Gevaert,
MD, PhD
ENT specialist, Department of Otorhinolaryngology, Ghent University Hospital (Belgium)

“For me, personalised medicine is a combination of clinical observation and advanced diagnostics. I am an ENT surgeon, but I do quite a lot of research in allergy in the nose. I have witnessed, for more than 20 years, that component-resolved diagnosis alone – measuring just one element or multiplying omics – can't give us the answer. As physicians, we know that patients often present combined problems. For example, as an ENT surgeon, when I study a patient's nose, I can see that the patient has an obstruction of the nose because of a house dust mite allergy, but the patient can also have sinusitis or a septal deviation. And there might be more problems than just those.

If we only focus on omics and advanced diagnostics, in my opinion, we are missing something. Thanks to artificial intelligence and big data, we can combine omics and advanced diagnostics with what we find in a medical file. We observe how important clinical findings and comorbidities are for diagnosis and predicting outcomes. As a physician, I think this combination is both the foundation for personalised medicine and the best solution for the patient.”

ALLERGIC PATIENTS



CLINICAL DATA

- Age
- Gender
- Lifestyle
- Comorbidities
- Environment
- Treatment response



OMICS DATA

- Genomics, proteomics, etc
- Identification of biomarkers which enable disease diagnosis



PHENOTYPE CHARACTERISATION

- Identification of clinically observable features of each individual which determine how likely they are to respond to treatment



ENDOTYPE CHARACTERISATION

- Identification of the individual mechanism of disease and pathophysiology of the disease



ALLERGIC PATIENTS SUBGROUPS

Market *environment*

The number of people with allergies has risen continuously over the past 60 years, with higher incidence rates among children. Today, more than one billion people worldwide are affected by allergies, and it is expected that by 2050, 1 in 2 people will suffer from allergies¹.

Rapidly increasing prevalence

The increasing prevalence and intensity of allergies is a trend that has continued in the industrialised world for more than 60 years. Allergies currently affect over 13% of the world's population, and an estimated 20% to 30% of the developed world².

Allergies impact quality of life and can trigger asthma

The limitations resulting from the body's reaction to allergens are multifaceted but share one common theme: the patient's quality of life is no longer what it used to be.

People who are sensitised to aeroallergens develop allergic rhinitis with symptoms such as a runny nose, itching, watery eyes, respiratory congestion and fatigue. A possibly less well-known and often underestimated consequence is that allergies put people at a greater risk of developing asthma.

People with allergic rhinitis are three times more likely to develop asthma than other people, and the risk for patients with house dust mite-induced allergic rhinitis is about six times higher than those whose allergic rhinitis is caused by grass pollen².

Too many patients are not treated

Allergic rhinitis affects approximately 10% to 30% of adults and 40% of children². Only approximately 12% of people suffering from allergic rhinitis are treated with allergen immunotherapy (AIT) products due to low awareness among primary care prescribers, a complex treatment pathway and a market that is dominated by lower cost symptomatic treatments. AIT is the only treatment that addresses the underlying cause of allergy and may provide both rapid (within a few weeks) and long-lasting improvement of all symptoms, whereas symptomatic treatments (such as antihistamines and corticosteroids) temporarily relieve some allergy symptoms.

With a modest proposal rate, the AIT market is still underdeveloped, representing approximately €1bn or 12% of the global allergic rhinitis market and is expected to grow by 2% annually in the coming years³.

Market growth is expected to result from an increased awareness of respiratory allergies, easier access to allergists, the expanded range of administration modes as well as a growing middle class in developing countries that will gain access to medical treatment.

1. Bousquet, J., Burney, P.G., Zuberbier, T. et al. (2009). GA2 LEN (Global Allergy and Asthma European Network) Addresses the Allergy and Asthma Epidemic. *Allergy*. 64: 969–977
 2. World Allergy Organization. "White Book on Allergy: Update 2013" — 3. Market size (€1bn) and expected growth (2%): global data and internal estimates share of AIT market in the global allergic rhinitis market (12%): Visiongain report 2018.



Climate change and allergies

Isabella Annesi-Maesano

Director of Research at INSERM (the French National Institute for Health and Medical Research), Deputy Director of the Desbrest Institute for Epidemiology and Public Health, INSERM-University of Montpellier

Why is climate change an important aspect of allergology?

Climate change affects the disease pathology both directly and indirectly. Temperatures, humidity or atmospheric pressure have a direct effect on the disease; humidity, for example, has a significant impact on asthma. And, by impacting the risk factors for allergic diseases (pollen, mould, allergen proliferation, chemical air pollution), climate change has an indirect influence on allergic diseases and can contribute to the development of childhood asthma or cause severe complications for people with asthma.

Increased pollution levels linked to soil desertification, forest fires, urbanisation and traffic, fossil fuel production, etc. also affect the molecular structure of pollen. Air pollution, by damaging the outer membrane of pollens, causes pollens to release microparticles which harm our mucous membrane and bronchial airways and can, in turn, trigger asthma. Pollens become increasingly allergenic as a result of climatic conditions and increased CO₂ levels; when CO₂ increases, plants produce more pollen and, notably, pollen with a higher allergenic potency.

We have been studying the evolution of allergens in relation to climate change for many years now. For example,

for pollen, botanists have collected a lot of data and pollen count series that show the evolution linked to climate change. Pollens are increasing, plants are migrating geographically, depending on the climate, and adapting their molecular structure to go where it is better for them in terms of pollination with longer seasons and earlier in the year (February instead of March). We also have similar data on moulds and mites.

What role does the exposome play on the health of each individual?

I have been working on the exposome for quite some time now. The exposome is the set of environmental risk factors (e.g. physical, chemical, biological, dietary, climatic or geographical, social, economic or contextual) an individual is exposed to throughout his or her entire life and the interactions of which may or may not lead to the development of a pathology. Obviously, each individual's genetic profile plays a role in the development of pathology but not all diseases are monogenic and, in particular, asthma and allergies are multifactorial and multigenic.

In allergology, we are quite advanced on these issues because we have been studying them for a long time. All the environmental factors potentially involved are taken into account and treated by big data, artificial

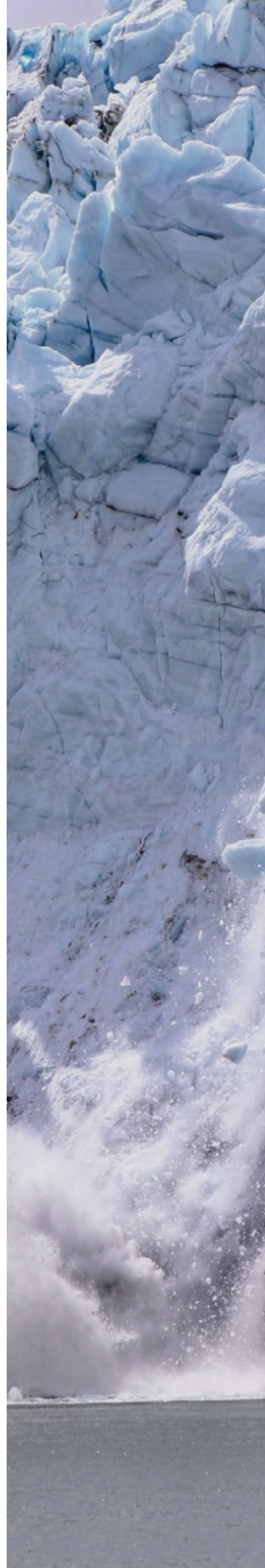
intelligence, etc. We have made more progress in the field of allergic diseases than in other disciplines because it is a multidisciplinary science involving clinical observations as well as all the sciences related to exposures (allergens, botany, etc.).

To this set of environmental risk factors should also be added the consideration of crucial periods in the life and development of the individual (pre-conception, pregnancy, first 100 days, adolescence, menopause, old age etc.).

Why take an interest in this and consider these interactions?

Because we are dealing with multifactorial diseases and we can thus identify a risk profile that is useful for both understanding allergic diseases and their prevention. Moreover, this work has made it possible to identify avoidable exposomes on which we can act through prevention measures.

We must not forget that the World Health Organisation insists on the importance of identifying the "vulnerable populations", i.e. individuals who are particularly weakened by inequalities and who must be taken into account by the public authorities in order to be protected.



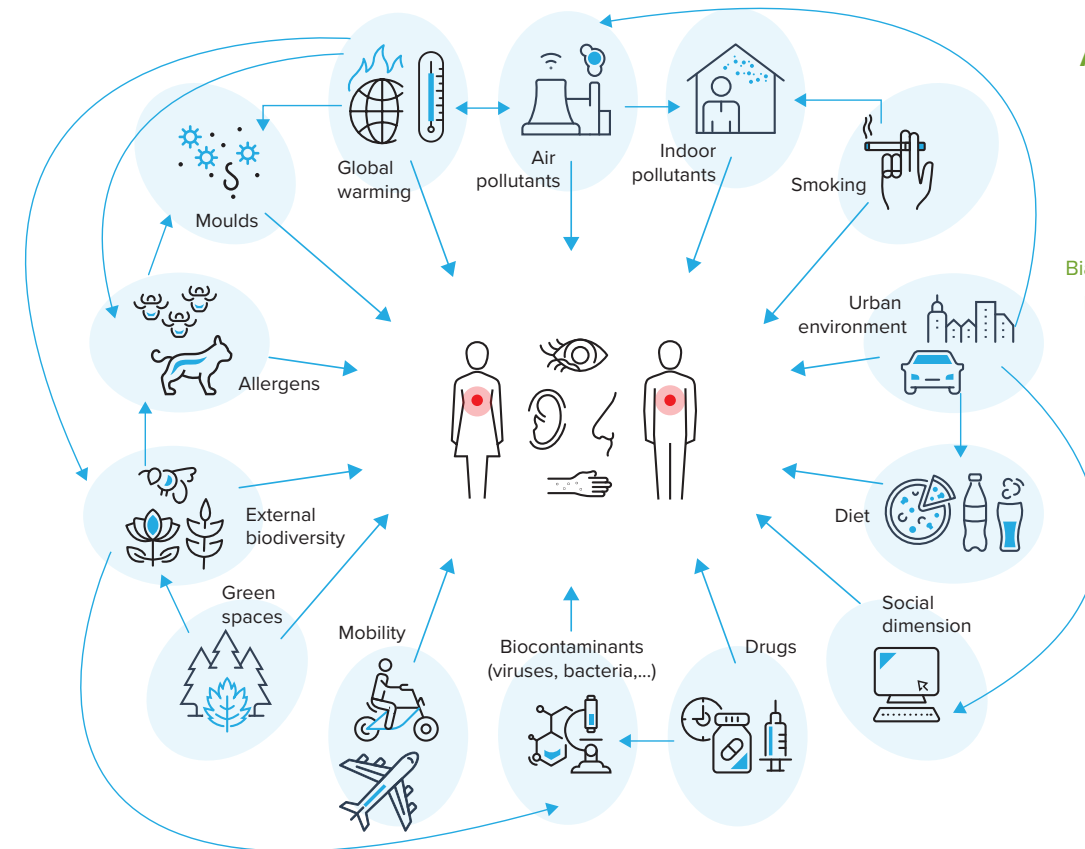
Innovation in science and technology is creating new medical opportunities

Biologics, gene therapies and other new molecularly targeted compositions are starting to deliver on their promise to enable more precise diagnostics and more tailored treatments. The increasing development of patient-friendly treatments (shorter treatment lengths, ease of use) should improve AIT penetration in the allergic rhinitis patient population and their adherence.

In addition, advances in the areas of genetics and informatics are driving a transformation in our understanding of the disease. Innovations in technology also present opportunities to address the growing volume of regulatory requirements more efficiently and more effectively.

Rise in allergies gaining attention from payers, providers and regulators

As more patients seek treatment for their allergies, the AIT industry has gained greater attention from the healthcare community. Healthcare providers are seeking more clinical evidence related to the safety and efficacy of AIT; payers are tightly controlling access and increasingly requiring data about the economic benefit to maintain coverage for treatment; and regulatory bodies are intensifying their scrutiny and enacting more stringent requirements of biologics manufacturers.



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Call to action: Air pollution, asthma, and allergy in the exposome era

Isabella Annesi-Maesano, MD, PhD, DSc, Cara Nichole Maesano, PhD, Benedetta Biagioni, MD, Gennaro D'Amato, MD, Lorenzo Cecchi, MD, PhD

Allergens

An allergic reaction is an inappropriate response by the body's immune system to foreign substances, or allergens, such as house dust mites, pollen, food, mould or pet dander. Allergies are a common, chronic, often debilitating condition that often affects the patient's quality of life and can sometimes even cause a fatal reaction.

HUMAN ALLERGIES

Potential allergy symptoms in humans cover a variety of symptoms which can range from mild to severe. Symptoms vary from one person to another and according to the allergy. If left untreated allergy symptoms can worsen over time.

- Psychological symptoms: fatigue, irritability, poor sleep, negative effect on concentration and performance
- Allergic conjunctivitis with itchy, red and watery eyes
- Allergic rhinitis with sneezing and blocked or runny nose
- Swelling and itching in the oral area
- Suffocation by swelling of the throat and larynx
- Allergic asthma with dry cough and shortness of breath
- Skin or digestive discomfort
- Wheezing
- Constricted airways in the lungs
- Severe lowering of blood pressure and shock

Grasses

Grasses are one of the most common causes of allergies. The pollen released by grass can be carried by the wind over many miles.



Trees

Tree pollen is the first seasonal allergy of the year, with some trees releasing pollen in January. Trees that trigger allergies include ash, beech, birch, cedar, elm, mulberry, olive, poplar, willow, etc.



Air pollutants

Traffic-related emissions are a significant source of air pollution and can worsen allergic rhinitis symptoms and asthma. Industrial air pollutants and particulates can exacerbate allergic rhinitis and asthma as well as modify the allergenic potential of certain pollens.



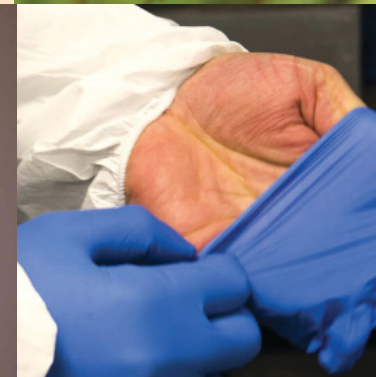
Weeds

Weed pollen season occurs from spring to early autumn. Weeds that trigger allergies include mugwort, nettle, lamb's quarters, ragweed, sage, Russian thistle, etc.



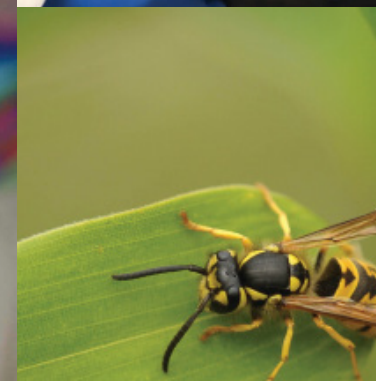
Latex

Natural rubber latex, the protein in the sap of the Brazilian rubber tree, is found in many consumer goods (balloons, rubber bands, etc.). Latex allergy symptoms may include hives, itching, stuffy or runny nose. It can cause asthma symptoms with difficulty breathing and can result in anaphylaxis.



Insect venom

Insect venom stings can cause severe reactions in people with allergies. While some will have only minor reactions to stings, others may have a life-threatening allergic reaction and go into anaphylactic shock. Venoms responsible for allergic reactions include species from the Hymenoptera order including honey bees, hornets, wasps and yellowjackets.



Food allergies

The most common food allergies are triggered by milk, egg, peanut, tree nut, soy, wheat, fish and shellfish. While most symptoms from food allergies are mild and limited to skin or digestive discomfort, some people may develop anaphylaxis which can lead to constricted airways in the lungs, severe lowering of blood pressure and shock and suffocation by swelling of the throat and larynx.



House dust mites

House dust mites belong to the Arachnida class, which includes spiders and ticks. They measure between 0.2-0.4 mm and are present in all households where they tend to be more numerous in bedding, upholstery, carpets, etc.

Pets

Animals with fur can be a source of allergy. The body reacts to dead flakes of skin shed by animals. What triggers an allergic reaction isn't pet fur, but a substance found on the pet's fur; this allergen is produced by the skin of felines and is also present in their saliva, urine, tears and dander.



Mould, mildew

Fungi can be found both indoors in damp areas (bathroom, kitchen, etc.) and outdoors (fallen leaves, compost, grasses, etc.). The spores produced by the fungi are released by wind and dew.



VETERINARY ALLERGIES

Animals can suffer from many of the same ailments as people, including allergies. Most allergies in animals fall into three categories: environmental allergies, food allergies, and insect-bite allergies. Allergies in animals can have a significant impact on quality of life and can greatly strain the relationships between people and their companion animal.

Some signs of potential allergies in companion animals such as dogs, cats and horses (symptoms vary according to species):

- Itchiness: excessive scratching, licking, chewing themselves, overgrooming, rubbing against trees, fences, stalls or rolling in the dirt or grass to "scratch their itch". Red, inflamed skin, small scabs or crusts on the body
- Fur loss
- Frequent, recurrent ear infections
- Frequent, recurrent anal gland problems
- Hives
- Digestive discomfort
- Sneezing and runny nose
- Runny eyes
- Cough



Patient journey

Respiratory allergies follow a chronic and progressing disease course, especially when left untreated¹. Allergic rhinitis is often under-diagnosed and from onset of symptoms, a patient may have waited eight years to see a specialist².

Globally, over **400 million people**³ suffer from allergic rhinitis

Asthma and allergic rhinitis are estimated to result in more than

100 million⁴ lost workdays and missed school days every year

Patients may have waited **8 years** to see a specialist²

Allergen immunotherapy is used in **less than 10%**⁵ of eligible patients

1. Bousquet J, et al. Allergy 2008;63(S86):8-160 - Canonica GW, et al. World Allergy Organ J 2008;1:138-44 - Valovirta E. EFA Book on Respiratory Allergies - Raise Awareness, Relieve the Burden. www.efanet.org — 2. Valero A. Et al. Am J Rhinol Allergy 2011 — 3. Canonica GW. Etb al. Allergy 2007;62 (suppl. 85) — 4. The European Academy of Allergy and Clinical Immunology Advocacy Manifest — 5. Jutel M, et al. J Allergy Clin Immunol 2015;136:556–68

SYMPTOMS

- Itchy, red and watery eyes
- Sneezing, itchy, blocked or runny nose
- Swelling and itching in the oral area
- Allergic asthma with dry cough and shortness of breath

Symptoms become persistent and begin to cause fatigue, irritability, poor sleep and can have a negative effect on concentration and performance

Symptoms fail to improve and patient experiences only temporary relief from self-care and over-the-counter treatments.

After symptomatic treatment cessation the patient continues to experience discomfort.



Patient seeks online support, uses avoidance measures and home-care products to help relieve symptoms.

Patient seeks help from pharmacist, uses over-the-counter treatments, nasal sprays and/or dermatological products^{6, 7}.

Patient seeks help from healthcare practitioner who, following an initial diagnosis, prescribes symptomatic treatment. Should symptoms continue or worsen after treatment, general practitioner refers patient to an allergy specialist.

Patient consults an allergy specialist who carries out the diagnosis of allergy based on clinical history, physical examination, allergy tests and specific questions. Once the allergen is identified, three treatment options are proposed: allergen avoidance, symptomatic treatment (antihistamines, corticosteroids), desensitisation through allergen immunotherapy when symptoms are not adequately controlled with pharmacotherapy and/or the patient seeks sustained effects⁸.

6. Didier A. et al. optimal dose, efficacy, and safety of once-daily sublingual immunotherapy with a 5-grass pollen tablet for seasonal allergic rhinitis. Allergy Clin Immunol. 2007, 120: 1338-1345. — 7. Moingeon P, et al. Immune mechanisms of allergen-specific sublingual immunotherapy. Allergy 2006;61:151-65 — 8. Peter Hellings et al. Rhinology 2020, and Professor Glenis Scadding et al., WAO Journal 2020

Our diagnostic and therapeutic *solutions*

Stallergenes Greer supports allergists and patients at each stage of allergen immunotherapy treatment. Our comprehensive and consistent portfolio is adapted to the individual needs and profile of each patient and covers a broad variety of allergens.

Spanning source materials, routes of administration, cutting-edge delivery mechanisms and finished products, Stallergenes Greer's innovative diagnostic tools and allergen immunotherapy (AIT) solutions are designed to improve ease of access and treatment outcomes.

Diagnosis

The diagnosis of respiratory allergies is based on clinical history, physical examination, allergy tests and specific questions. One of the diagnostic methods used by medical practitioners to identify the triggering allergens in patients is a skin prick test.

Via a prick to the skin, the patient is exposed to the suspected allergen and is monitored. After approximately 20 minutes, the skin is observed for any signs of reaction to one or several of the allergens: redness, swelling, itching.

Stallergenes Greer offers a broad portfolio of testing extracts which allow to test for a wide range of allergies. The company also offers testing devices.

Allergen immunotherapy

AIT is an allergy treatment designed to treat the underlying cause of the disease as well as have a long-lasting effect on all symptoms. After an accurate diagnosis of the type of allergy and responsible allergens, patients, in line with their healthcare practitioner's prescription, receive a targeted treatment, available either in sublingual (tablets or drops) or subcutaneous (injections) form depending on product availability in each country.

Because it treats the root cause, AIT results in immunologic tolerance; i.e. a decrease in the body's reaction to an allergen. Through the repeated administration of specific allergens to patients, the immune system builds resistance by changing the types and proportions of antibodies (immunoglobulins) and proteins (interleukins) it produces when it is exposed to the allergen, thus reducing symptoms when patients are exposed to the allergen in their environment – even after treatment ends. AIT usually requires 3 to 5 years of treatment¹.

1. Marogna M. et al., Long-lasting effects of sublingual immunotherapy according to its duration: A 15-year study. J Allergy Clin Immunology, 2010)

Our products

Whatever the options, Stallergenes Greer's diagnostic and allergen immunotherapy treatments meet the most stringent clinical criteria, quality standards and health authorities' regulatory requirements.

The market availability of Stallergenes Greer's treatments varies according to each country.

Named patient products

Stallergenes Greer believes one solution does not fit all patients, hence we provide patients with personalised treatment options that are tailored to their individual needs. We aim to offer a comprehensive portfolio of AIT treatments globally which allow patients and their physicians to determine the administration method that best meets the disease and lifestyle needs of the patient.

The company's allergen extracts cover a vast array of allergens. They can be produced in standardised form and can also be tailored to the specific needs of patients in terms of composition, concentration and dosage.

These personalised solutions, known as Named Patient Products (NPPs), are prepared according to the allergist's prescription and the patient profile using a stock solution obtained via the extraction of allergens (pollens, house dust mites, moulds...). Each NPP has its own biological activity and is prepared for the unique needs of an individual patient.



Sublingual

Staloral® (oral drops), for the treatment of allergy involving rhinitis, conjunctivitis, rhinoconjunctivitis or asthma (mild to moderate) of a seasonal or perennial nature, in adults and children (from the age of 5).

Actair®/ Orylmyte® (tablet), for the treatment of house dust mite allergies involving rhinitis, with or without conjunctivitis, in adults and adolescents over 12 years (and under 12 in certain territories).

Oralair® (tablet) contains a five-grass (sweet vernal, orchard, perennial rye, timothy, Kentucky blue grass) mixture, which represents many of the natural exposure and sensitisation conditions of grass pollen allergic patients.

Subcutaneous

Alustal®, for the treatment of allergic rhinitis, allergic rhinoconjunctivitis or mild to moderate asthma in adults and children.

Albey® venom, for the treatment of allergy to wasp, honeybee, and yellow jacket venoms.

Extracts and supplies

Stallergenes Greer manufactures a broad portfolio of allergen extracts and diagnostic tests.

- Bulk extracts
- Testing supplies : **Alyostal Prick®**, **Stallerpoint®**, **Prick Lancet®**, the **Greer® pick® system**, **Greer® pick®**, **Greer® pick® well™**, **Greer® pick® tray™**, **Greer® pick® tray™ lid**, **40-well Greer® pick® evaluation package**, **60-well Greer® pick® evaluation package**, **Skintestor Omni™system**, **Skintestor Omni™**, **Skintestor Omni™ trays**, **40-well skin Omni™ evaluation package**, **60-well Skin Omni™ evaluation package**, **IVD (in vitro diagnostic test)**, **CADALAC Veterinary diagnostic test**

- Source materials and other supplies (sterile diluents, vials)
- **GREER® Extracts™** extracts are USDA approved for both subcutaneous and sublingual administration for veterinary use. Stallergenes Greer offers a wide selection of extracts and formulations.
- **GREER® Sterile Diluents™** various sizes, formulations, and fill volumes available.
- **GREER® Sterile Empty Vials™** a range of industry-relevant sizes for extract mixing and storage.

Veterinary use

From allergen testing to making precision treatment medicines, Stallergenes Greer is committed to providing veterinary specialists with products that can help treat animal allergies.

In the U.S., Stallergenes Greer offers a comprehensive range of allergen extracts and supplies for veterinary dermatologists to support the needs of their clients and pet patients.

Veterinary dermatologists are veterinarians that have specialised training in the management of allergic disease. They may use products from companies like Stallergenes Greer to compound named patient allergy products for dogs, cats, horses, and more.

Stallergenes Greer produces extracts of different strengths and formulations specifically for veterinary specialists.



What we do

From nature to *high quality* allergen immunotherapy solutions

At Stallergenes Greer, we have more than 100 years of experience in the field of allergies and allergen immunotherapy. Our large range of allergen extracts are derived from natural sources (pollens, grasses, house dust mites, venoms, etc.) using state-of-the-art technologies to provide patients with high quality allergen immunotherapy treatments adapted to their needs and profile.

Working with nature

We are committed to providing patients with high quality allergen immunotherapy products. To achieve this, we have adopted an integrated approach to the sourcing of our source materials, the production of our treatments and their distribution. Prior to the extraction of the allergens, we select and harvest the raw material which guarantees both the quality and the reproducibility of the allergenic extracts.

For house dust mites, for example, we grow the two key species responsible for allergies: *Dermatophagoides farinae* (American house dust mite) and *Dermatophagoides pteronyssinus* (European house dust mite) at our Antony (France) site. The mites are grown on a nutrient medium, Stalmite APF®, which contains no animal and/or human-derived material thus preventing any risk of transmission of pathogenic transmissible agents, using a process that retains both the bodies and faeces of the mite. This ensures that our extract mimics natural exposure to the allergen. Growth conditions are strictly controlled to ensure consistency and quality of these products (e.g. kinetics and metabolism).

For grass, we grow five species of grasses (sweet vernal, orchard, perennial rye, timothy, Kentucky blue grass) on 90 hectares of land in Amilly (France). These grasses represent many of the natural exposure and sensitisation conditions of grass-pollen allergic patients. The pollen is harvested using specifically designed combines equipped with a patented vacuum harvesting system. The harvesting technique and post-harvesting processes ensure that the source material consists of

mature pollen grains and that all the targeted allergens are obtained. The pollen is purified on site before being transferred to our Antony (France) facility. In the U.S., our facility in Mathiston, Mississippi, grows, harvests and collects over 75 different types of pollen on more than 56 hectares of land.

For mould, the mycology department in Lenoir (North Carolina, U.S.) prepares fungi, and only fungi, for extraction. Unlike allergens obtained from external sources, fungi from Stallergenes Greer are grown entirely in our North Carolina facility from authenticated cultures. They are cultured on specific growth media under strictly controlled conditions to ensure quality and consistency. The mycology department can grow more than 60 different fungal cultures. To assure long-term supply and safety stock, we maintain stock cultures of our moulds, stored as either oil overlays or lyophilised plugs.

Allergen characterisation

The characterisation of allergen extracts notably aims to identify the allergen's molecular structure, IgE binding properties and its allergenic potency. Extracts are characterised using highly advanced analytical technologies. These technologies allow both a precise quantification of the composition of our products and intermediates at all stages of the process as well as the molecular physico-chemical integrity of personalised allergen preparations. Quality control is carried out at every stage of the process, from the arrival of the source materials through the various production stages to the market release of the finished personalised product.

1. Moingeon P, et al. Clin Exp Allergy Rev 2008;8:12-4

Our science

Precision medicine is the focus of Stallergenes Greer's strategy. We are committed to promoting progress and developing precise and personalised therapeutic solutions which are tailored to the individual profile and needs of each patient.

A high level of scientific expertise

Allergen immunotherapy (AIT) is the only therapeutic class capable of modifying disease progression and potentially preventing the onset of the disease. AIT consists in administering allergens by sublingual or subcutaneous route, thus allowing the reorientation of the immune responses of patients towards allergen-specific tolerance induction.

We focus our efforts on allergen characterisation as well as on optimal approaches to deliver allergens to the immune system. Each allergen source contains several molecules which are recognised by the immune system as allergens and will trigger an allergic reaction.

Allergens are large, complex molecules. Working with large molecules requires a high level of scientific expertise and state-of-the-art technologies to characterise and quantify allergens. Specific processes are required due to both the complexity of the molecules and their biological nature.

Focusing on precision medicine to advance personalised solutions

Stallergenes Greer boasts a long-standing expertise regarding the mechanism of action of AIT and has been intensifying the identification of biomarker candidates to predict and monitor the efficacy of the company's AIT treatments.

Our research has allowed us to identify pro- allergenic cells, such as Th2A –T helper cells that are involved in the production of IgE (immunoglobulin E, antibodies produced by the immune system when it reacts to certain substances) as a therapeutic target for AIT. We continue to work towards identifying the most relevant allergens for the treatment of allergies and partner with renowned academics in the field of respiratory allergies to characterise the molecular profiles of allergic patients.

Clinical development and real-world studies

Stallergenes Greer has conducted a large number of clinical studies, involving more than 9,000 patients, to provide evidence that our AIT treatments are both safe and effective and to produce high-quality data for decision-making.

A real-world approach is also increasingly being used by Stallergenes Greer to further evidence AIT treatments beyond clinical trials. Since they are based on large populations of patients, real-world studies provide useful data to optimise AIT prescription and clinical performance. Real-world studies include larger patient populations which better reflect “real life” patient profiles. The Group’s BREATH programme, launched in 2017, showed both positive results regarding the efficacy of sublingual tablets in respiratory disease and real-world evidence that patients with allergic rhinitis achieve control of their respiratory disease with fewer allergic rhinitis prescriptions and less need for symptomatic medication^{1,2}.

Stallergenes Greer has four real-world studies underway:

- CORAP: to evaluate the impact of AIT on the quality of life of patients and other relevant patient reported outcomes.
- EfficAPSI: to document the public health value of named patient products over the long term and for a wide range of allergens. More than 200,000 patients will be included in this retrospective observational study which analyses the effect of allergen immunotherapy on the occurrence or worsening of asthma, and the use of associated medication.
- MaDo: to retrospectively analyse the needs, reasons, modalities and impacts of AIT dose adjustment.
- PRACTIS: which aims to evaluate the benefits of sublingual AIT in current practice according to the different methods of use and the type of allergen.

A collaborative approach to innovation

Stallergenes Greer leverages open innovation to continue to advance precision medicine for the benefit of patients and healthcare practitioners.

The Group recently entered into a research collaboration on the discovery of biomarkers of AIT efficacy with Imperial College London. The collaboration will contribute to both deciphering the mode of action of AIT and identifying key markers that can be used in the routine practice of allergology. Based on the understanding of specific phenotypes and the responses of patients with allergies, allergists will be able to tailor treatment modalities with the right dosing at the right time for each individual.

In 2021, Stallergenes Greer also signed a partnership with Alyatec, a contract research organisation based in Strasbourg University Hospital (France). The collaboration, which focuses on allergy pathophysiology and endotypes, AIT mode of action and clinical validation, will build on Alyatec’s competencies in research and clinical services as well as its state-of-the-art technology, including a new generation environmental exposure chamber.

1. P. Devillier et al. Allergy 2018; doi: 10.1111/all.13705 — 2. S. Zielen et al. Allergy 2019; 73:165-77



Professor Frédéric de Blay

Principal investigator and Medical expert of Alyatec - Head of the Thoracic Pathology Unit Strasbourg University Hospital (France) - Head of the Pneumology, Allergology and Environmental Respiratory Pathology Unit - President of the French Federation of Allergology

“Alyatec’s environmental exposure chamber allows to both accelerate drug development and improve patient characterisation.

The chamber is used to expose patients to an allergen to which they are sensitised: when an allergic reaction is triggered, the patient is given a drug or a placebo and the efficacy of the drug can be measured rapidly. If the drug shows limited efficacy in the chamber, we know that it won’t work in real life either. This allows us to eliminate candidate molecules fairly rapidly.

The chamber also contributes to improving patient characterisation to, for example, discover which patient will best respond to desensitisation. When a patient with asthma has an asthma attack in the 30 to 60 minutes following exposure or develops another respiratory symptom in the 3 to 12 hours following the immediate response, we know that these patients produce more eosinophils and may be good candidates for desensitisation.

We have made significant progress in recent years and exposure chambers have a part to play in advancing allergen immunotherapy.”

Technical operations

Our teams work around the clock to make sure that patients and healthcare practitioners receive the highest quality diagnostic solutions and allergen immunotherapy treatments, on time, every time.

Products derived from living systems

Like other biologic drugs, Stallergenes Greer's allergens are derived from living systems. Biologic drugs contain one or more active substances that are produced in a living system such as micro-organisms and plant or animal cells¹. Biologics consist of large and complex molecules; their characterisation is challenging and involves highly advanced technologies. They target specific cells in the immune system.

A patient-centric approach

Because Stallergenes Greer's allergen immunotherapy (AIT) treatments cater to the real needs of patients, product design begins with a clear understanding of patient profiles: to which specific allergen is a patient exposed, to which allergen(s) is a patient sensitised and is the allergen clinically relevant.

Quality, safety, controls at every stage

To provide patients with the benefits they need, controlling the quality of allergen products is of prime importance to guarantee both the safety and efficacy of allergy diagnosis, AIT and consistent optimal clinical benefits².

Stallergenes Greer's allergens are manufactured in a living system and their production is strongly process-dependent. To ensure batch-to-batch consistency, quality and purity of its products, Stallergenes Greer has established stringent controls of the source and nature of the source materials and applies hundreds of process controls to ensure that target quality attributes are delivered. Each batch of product is the combination of the product, documentation and controls.

Consistent biological potency through process standardisation

Stallergenes Greer ensures the consistent biological potency of its tablets, sublingual and subcutaneous products through standardised and validated quantitative analytical methods which assure the uniformity and purity of the Group's products and their activity.

Driving operational excellence

We seek excellence in every part of our organisation. Our approach to manufacturing quality products relies on continuous learning and improvements to ensure we are continually modernising our quality controls and improving our processes through investments in our facilities.

Having the right product available is critical to ensuring patient's needs. We rigorously manage our operations to ensure product availability by focusing on operational excellence and investing in state-of-the-art equipment, technology, and systems. Our manufacturing facilities in France produce individual treatments that are delivered directly to patients. In the U.S., our bulk allergen extracts are delivered to medical practitioners who prepare the individual treatment for their patients.

Accelerating pharmaceutical development

To offer patients with allergies the best treatments and ensure that we stay at the forefront of AIT, we make specific efforts to optimise process development and formulation as well as continuously acquire increased knowledge of our molecules and processes.

1. Biological product definitions www.fda.gov – 2. Zimmer J, et al. Standardization and regulation of allergen products in the European Union. *Curr Allergy Asthma Proc* 2016;16(3):21.

North America

Maintaining *robust positions* in a challenging marketplace

Throughout 2021, Stallergenes Greer Americas focused on its key strategic pillars to position the business for sustainable long-term growth while delivering high quality services to its stakeholders.

Committed to sustainable long-term growth

Stallergenes Greer, true to its core values of superior customer service, high quality allergen extracts and a legacy of commitment to the specialist community, showed perseverance in overcoming the challenge of the pandemic and continuing to deliver on its purpose.

In 2021, in a competitive marketplace still impacted by the effects of the pandemic, Stallergenes Greer posted stronger top line growth, fuelled by robust performance of human subcutaneous allergen immunotherapy and veterinary segments, whilst maintaining strong positions across all its businesses.

Focusing on supply, quality and operational excellence

As part of its commitment to continuous improvement across its businesses, Stallergenes Greer maintained investments in its infrastructure, processes and people with a focus on supply, quality and operational excellence.



Significant advancements were made throughout the year with the implementation of a state-of-the-art ERP system to increase visibility into the company's processes, investments in manufacturing to drive quality while yielding higher product, and the development of a lean six sigma training programme for employees.

A trusted partner for its customers

After more than 100 years serving the allergy community in the U.S., Stallergenes Greer continues to be a trusted partner for its customers and is committed to empowering healthcare providers to restore quality of life for people and pets with allergies.

This year, the region again delivered on its promise of next day delivery and developed a series of initiatives to support its customers in an environment still impacted by the COVID-19 pandemic. Stallergenes Greer's teams were ready and available to assist healthcare professionals to resume their practice and provided medical information, product consultation and training of allergen immunotherapy practice management.

The company continued to offer flexible payment agreements for healthcare professionals and maintained its co-pay assistance programmes for certain patients with a valid Oralair® prescription.

Strengthening market positions in the U.S. veterinary business

With the rise in pet adoptions still strong in 2021, the veterinary business maintained its solid position with veterinary dermatologists throughout the year. The U.S. teams launched a number of innovative projects to: further improve awareness and management of allergies in pets via initiatives to raise the understanding of the role and value of veterinary dermatologists, support veterinary teams in helping pet owners care for their pet with allergies, and provide education to better understand allergen immunotherapy.

The laboratory teams in Lenoir continue to innovate and advance our veterinary knowledge and extracts offering, including ongoing work achieving even greater consistency in our veterinary mite extracts and advancing understanding of cross reactivity between mite species in veterinary patients.

Canada: delivering growth while adapting to change

Despite restrictions imposed by the pandemic, Stallergenes Greer Canada posted robust growth in 2021 and ended the year slightly above its aspiration. The affiliate maintained stable delivery times throughout the year and continued to serve subcutaneous allergy patients on time, every time.

Sales teams took advantage of social distancing measures to create a virtual meeting space to share ideas, feedback and emerging trends from the field, which allowed the affiliate to develop cohesive messaging across the country and address new opportunities in a broader, more strategic and more agile manner.

Undeterred by limited face to face interactions with patients and healthcare professionals, Stallergenes Greer Canada broadened its reach and impact by converting many of its activities, patient education tools and interactions with physicians to virtual and online formats. The affiliate notably created a network of physicians to discuss interesting cases, best practices, challenges, and ideas. In small groups, they were able to exchange with colleagues that they wouldn't have interacted with in pre-COVID times.

Together with CSACI (Canadian Society of Allergy and Clinical Immunology), Stallergenes Greer Canada also sponsored the first "Women in Allergy" conference, connecting female allergists from across the country to discuss their unique challenges, to learn from each other and from inspiring female leaders from Canada and the U.S.

Europe and International

Delivering *results* while investing for the future

By any measure, 2021 was a successful and exciting year for the Europe and International region, marked by significant advancements across all territories.

Successful European registration and launch of house dust mite tablet

One of the major highlights of the year was the launch of Stallergenes Greer's sublingual house dust mite allergen immunotherapy tablet in a number of European markets. House dust mite allergies are among the most prevalent allergies and affect between 65-130 million persons globally¹.

In May 2021, the Group's house dust mite tablet received a positive outcome from the Paul-Ehrlich-Institut, Germany, which acted as reference member state on behalf of 21 European countries. At year-end 2021, national marketing authorisations had been granted in 20 European countries following the decentralised procedure. The tablet is registered in Europe under the brand names: Orylmyte®, Actair® and Aitmyte® is already available in Germany, Belgium and Luxembourg. Outside Europe, the tablet is registered under the brand name Actair® in Australia, Japan, New Zealand and South Korea.

The first country to launch Orylmyte® in Europe was Germany. This addition to the portfolio is a significant step forward for Stallergenes Greer which now offers a fully registered comprehensive portfolio for the benefit of all our stakeholders in the German market. The Group's portfolio will progressively be strengthened by the availability of the house dust mite tablet in countries where marketing authorisations have been granted. The enhancement of the portfolio represents a significant growth opportunity for the whole region.

Key business growth drivers and opportunities

In markets still affected by the impact of COVID-19, the Europe and International region continued to post top line growth, and to improve its profitability, with leading positions in more than 50% of the 37 countries in which it is present. Performance was primarily driven by Stallergenes Greer's core brands Staloral®, Oralair® and Actair® in the countries in which they are marketed.

Throughout the year, steps were taken to strengthen the region's sales force and continue to transform its' organisational structure. Stallergenes Greer now reaches a larger target audience and its brands Orylmyte®, Oralair® and Staloral® will fully benefit from this position in 2022. These changes were also made in the context of the ongoing Therapy Allergy Ordinance process in Germany which may result in the market exit of products representing a value of approximately €100 million.

In Italy, Stallergenes Greer expanded its portfolio with the relaunch of Alustal® and is well positioned to strengthen its market position as a result of the "regularisation" process which, similarly to the German market, may lead to market exit for non-registered products. In Spain, the Group also benefitted from the relaunch of Alustal® while gaining significant market share thanks to strong performances of Oralair®, Staloral® and Stallgoid® (an in-licensed subcutaneous allergoid from Diater). In the Nordic countries, a new distributor was selected; the effects of this operation are expected to be felt in the coming year. In North Africa,

Staloral® was granted reimbursement by Tunisian health authorities, and in Morocco operations were restarted following the selection of a new distributor. Middle Eastern operations remained impacted by the economic crisis in Lebanon.

Throughout the year, Stallergenes Greer continued to implement its expansion strategy. In Russia, the Group consolidated its position and invested in a clinical study for the potential expansion of Staloral® mugwort. Progress was also made towards entering China and other selected Asian markets, primarily with the Group's house dust mite tablet. In China, recent regulatory changes and market access possibilities contribute to market attractiveness and offer the potential to reach a significant number of patients with house dust mite allergies.

Investing in the growth of our people

Because our people are the driving force of our ongoing success, the Europe and International region pursued its commitment to the development of its teams and talents.

In order to adapt to a rapidly changing environment, the region introduced and implemented a portfolio of talent development tools including specific project management opportunities, temporary assignments, coaching, mentoring and apprenticeship initiatives, as well as tailored training programmes.

This toolbox of talent development initiatives, combined with detailed talent reviews carried out across all geographies, support employees both in their career development and in delivering on their business goals while enabling management to ensure succession planning and execution.

¹Respiratory allergy caused by house dust mites: What do we really know?, Moisés A Calderón, Allan Linneberg, Jörg Kleine-Tebbe, Frédéric de Blay, Dolores Hernandez Fernandez de Rojas, Johann Christian Virchow, Pascal Demoly

France

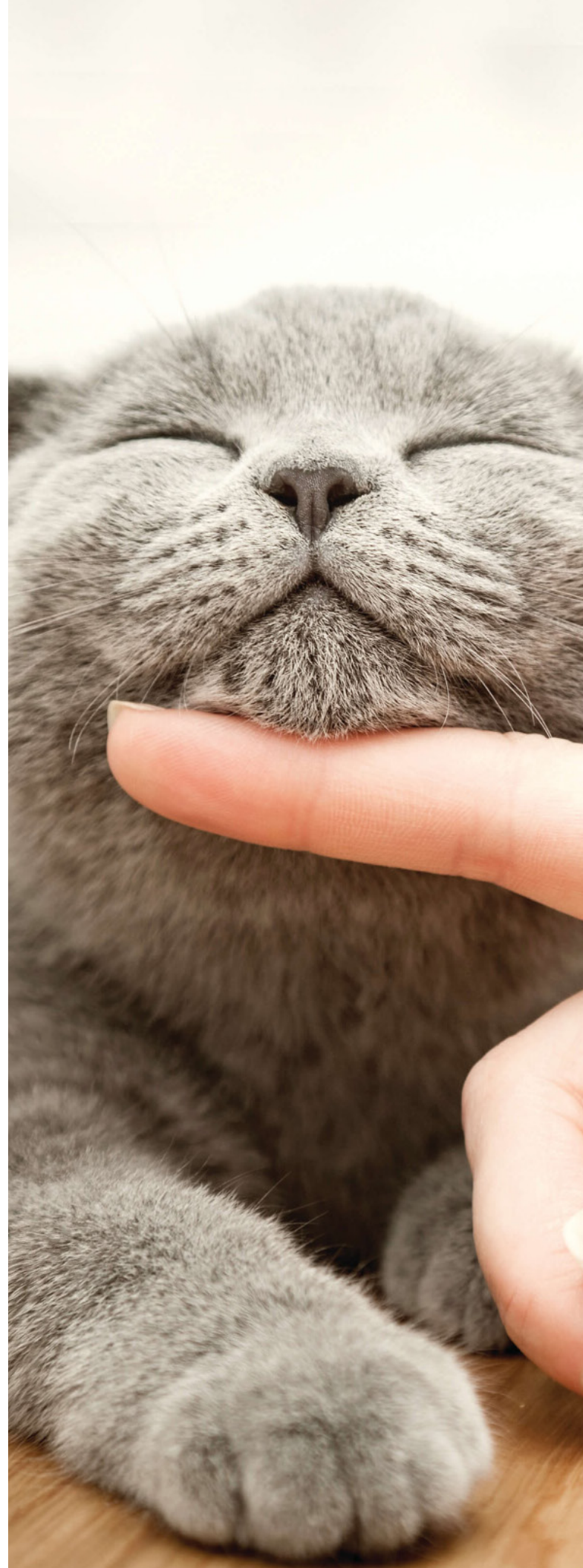
Leading the way in the French allergen immunotherapy market

In a competitive landscape, Stallergenes Greer's French operations continued to show strong growth throughout the year and consolidated leadership positions in the allergen immunotherapy market.

Leading the French allergen immunotherapy market

In 2021, Stallergenes Greer France further consolidated its leadership position in France (in terms of total market value and new patients within the allergy specialist space) with sustained commercial performances for Oralair®, Staloral® sublingual, and Hymenoptera venoms. The Group's Staloral® Cat 300IR and Staloral® Blomia references, launched the prior year, gained strong ground and showed promise in a French market still affected by the impact of the COVID-19 pandemic. The evolution of the sales force organisation to better support healthcare professionals in their daily practice contributed to the Group's robust performance in the French market.

This trend of growth is expected to continue in 2022, in particular with the launch of three new products: Orylmyte®, the Group's house dust mite allergen immunotherapy (AIT) tablet, Alustal®, the Group's injectable AIT treatment and the novel connected device for Staloral® on the French market in the coming months.



A personalised approach

Stallergenes Greer is committed to engaging with all its stakeholders to better serve patients and the medical community.

Among the initiatives which illustrate this commitment is the launch of Staloral® Cat 300IR in France. Sensitisation to cat dander affects up to 67% of people with asthma and there is a strong link between asthma and allergies to cats¹.

Because patient adherence to treatment is an important hurdle in the treatment journey, Stallergenes Greer also implemented a new personalised patient support service aimed at empowering patients undergoing AIT treatment. Once the allergen diagnosis and prescription have been made by the healthcare professional, patients who have accepted to be included in the service can be contacted by Stallergenes Greer's patient support services to obtain explanations, assistance and answers to any questions they may have regarding their treatment or its administration. This new service is available for patients throughout their treatment to address potential adherence issues. Patient and healthcare professional satisfaction were evaluated during the pilot phase of the service and the first results are very promising.

Contributing to improving access to care

Stallergenes Greer's commitment to patient care also encompasses the improvement of the care pathway for patients with allergies.

The increasing number of allergy sufferers highlights the importance of developing the care pathway and a multidisciplinary approach as the number of allergy practices in France is decreasing in certain regions.

Stallergenes Greer has, for example, been supporting SYFAL (the French association of allergists) in its endeavors to assist allergy specialists in opening their practice and optimising the efficiency of private practices.

Throughout the year Stallergenes Greer continued, via its Stall'Web online conferences, to foster dialogue with the allergy specialist community by sharing information, recommendations and scientific updates in the field of allergology.

Committed to addressing unmet medical needs

Allergy to cat dander is becoming increasingly common¹ with 30.5% of patients who suffer from allergic rhinitis sensitised to cat dander². Cat allergens are widespread allergens both in and outside the home where a cat has been present and their persistence can last for several months^{3,4}. It is estimated that the prevalence of cat allergy in patients who have never had a cat in the home may be as high as 34%⁴.

Each year, more than two tonnes of cat hair are collected to ensure the production of 10,000 allergen desensitisation vials in sufficient concentration.

After collection and processing, the source material is transported to the production site where it is analysed in accordance with European and French recommendations and its biological activity is measured. The large quantity of source material collected makes it possible to achieve the necessary allergen concentrations thanks to the implementation of adapted manufacturing processes.

Many months are required from the extraction of the source material to the availability of the finished products for patients. To ensure that Fel d 1 (the primary cat allergen) is present in allergenic preparations, it is measured throughout the manufacturing chain from source material to finished product. The treatment and extraction processes implemented by the Group ensure batch reproducibility and stability of the allergenic extract.

1. Rancé F. Allergy to animal dander in children. Archives de pédiatrie (Paediatric Archives). 2006; 13: 579-87. — 2. ANSES (French Agency for Food, Environmental and Occupational Health & Safety (ANSES). State of knowledge on the health impact of exposure of the general population to pollens in ambient air. Collective expertise report. January 2014. — 3. Lavaud F et al. Allergy to cat dander: the place of immunotherapy. French Review of Allergology 2013; 119-24. — 4. Davila I. Consensus document on dog and cat allergy. Allergy. 2018;73:1206-22.

Our people

Stallergenes Greer's 1,045 employees are at the heart of our Group. We foster a diverse and inclusive workplace that enables employees to perform at their best and offer opportunities for growth and talent development.



Our Ways of Working

Our Ways of Working embody our entrepreneurial mindset and create a high-performance culture where employees perform at their best.

Keeping it simple

Empowering

Focusing

Staying agile



A safe place to work

For Stallergenes Greer, the health and safety of our people is a constant concern. We care for the well-being of our colleagues and believe that high-quality working conditions are key to providing patients with the therapeutic solutions they need. Stallergenes Greer's Occupational Health and Safety Charter guarantees a safe and healthy working environment for all its employees and guides our practices.

Because the security of our people is paramount, Stallergenes Greer continually seeks to reinforce security measures at its various sites. In Antony (France), the Group notably carried out significant work with the installation of additional gates, turnstiles, cameras and signage, as well as increased communication regarding workplace security instructions and best practices.

Throughout 2021, we maintained our focus on keeping our colleagues safe by controlling risks,

implementing COVID-19 protocols and ensuring safety training programmes. While our manufacturing operations remained uninterrupted since the onset of the pandemic, staff working from home progressively returned on site during the year in line with local government regulations. Our colleagues rapidly adapted to digital conferencing and remote working conditions and were kept connected via a series of digital initiatives.

Talent development

As a high-performance company with an entrepreneurial mindset, Stallergenes Greer is committed to developing employees and offers a range of development and learning resources to support their growth. We encourage our employees to unleash their full potential and to continuously learn, develop and grow.

In 2021, in addition to the Group's bespoke training programmes to help strengthen role-based skills, Stallergenes Greer initiated a global talent management

programme with INSEAD. For this first session, 25 Stallergenes Greer colleagues from across the globe followed five weeks of training focused on management and leadership. Beyond skill and leadership development, the programme also aims to strengthen and develop a shared corporate culture. In 2022, the initiative will be broadened to an increasing number of employees.

Fostering engagement and dialogue

At Stallergenes Greer, we provide an inclusive work environment which embraces diversity and in which our people are recognised and supported to reach their full potential.

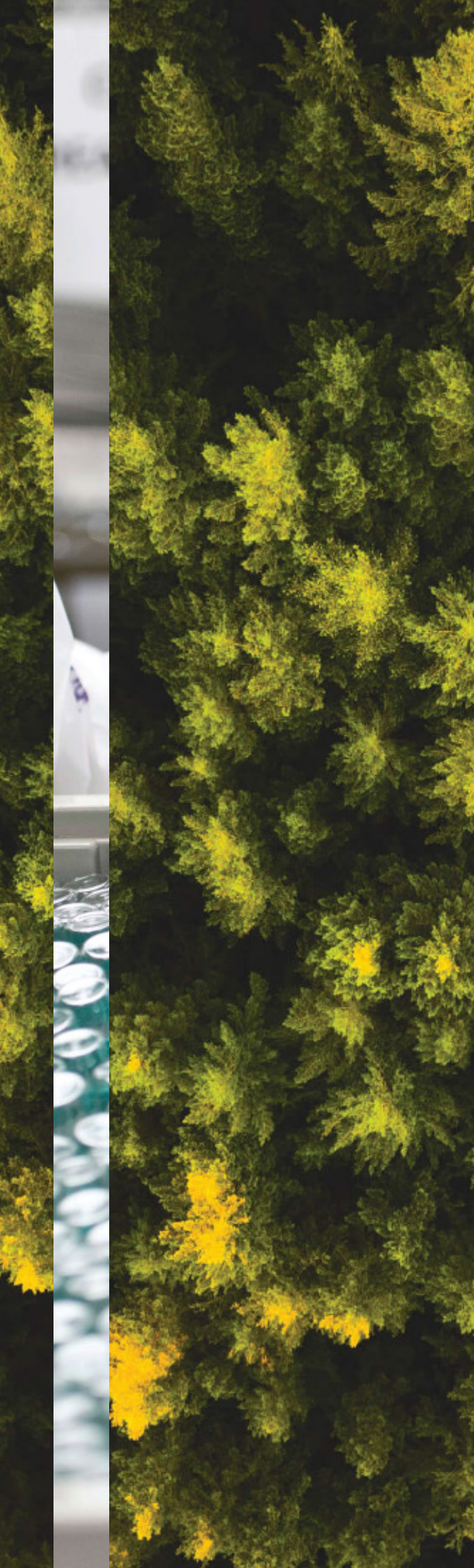
Throughout the year, a variety of initiatives and measures were developed across the Group to address employee needs and expectations and further develop our corporate culture. Increased communication and transparency, focusing on rewards and recognition are but some of the initiatives that were implemented throughout the year.

Giving back to our communities

We strive to have a positive impact in the communities in which we live and work. In an environment still marked by the COVID-19 pandemic, Stallergenes Greer continued to lend a helping hand with donations of personal protective equipment to healthcare professionals and donations to schools and disadvantaged families.

In France, we have partnered with Handiem, a non profit organisation dedicated to the employment of people with disabilities, to develop a mentoring programme which aims to support and promote the inclusion of disability in the workplace.

Our U.S. colleagues notably participated in "Sole Purpose", a fund raising project for a local elementary school, by donating shoes that could be repurposed to provide footwear for underprivileged children all around the world. The affiliate also provided an additional monetary donation. Employees in Lenoir, North Carolina also donated essential school supplies that were given to more than 200 elementary school students.



Our portfolio

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