



Annual Report 2012

Annual Report 2012



## Indicators





Net sales by therapeutic area











## 2

## **Relevant figures**

- 1<sup>st</sup> pharmaceutical company in Spain in R&D investment and 3<sup>rd</sup> out of all sectors.
- 1<sup>st</sup> dermatology prescription drug company in Germany and 7<sup>th</sup> in Europe.
- Drugs present in over 70 countries on the 5 continents.

## Talent at Almirall



**70 %** of employees expert in the pharmaceutical sector

**20**-plus different nationalities

20% of employees devoted to R&D

62 % of employees with university qualifications

**50%** Men Women

**14** years of experience at Almirall Spain on average

## R&D centres

• **R&D Centre of Excellence** in Sant Feliu de Llobregat (Barcelona, Spain) • Centre of Excellence for Inhalation (Bad Homburg, Germany) • Centre of Excellence for Dermatology (Reinbek, Germany)

#### Production plant

- Plant in Sant Andreu de la Barca (Barcelona, Spain)
- Plant in Reinbek (Germany)
- Plant in Sant Celoni (Barcelona, Spain)



# INDEX

- 6 Message from the President
- **10** Interview with the CEO
- 14 2012 highlights

## 17• ABOUT US

Mission, vision and strategic direction Corporate values Business model Stakeholders Corporate governance

## 29 • BUSINESS PERFORMANCE IN 2012

Highlights in R&D Strategic therapeutic areas Pipeline Patents R&D centres R&D partnerships Global reach of Almirall's drugs Growth platforms OTC products Corporate development agreements Business year sales Production

## 55• SOCIAL COMMITMENT

Our commitment to society Our team, Almirall's best asset Committed to health and safety and the environment

## **65** • FINANCE AND STOCK PERFORMANCE

Financial highlights in 2012 Functional Income Statement Balance Sheet Cash Flow Almirall on the Stock Exchange



Jorge Gallardo Ballart President

"Courage, leadership and commitment have led our management strategy in 2012. This helped boost our total revenues to over € 900 MM and generated a normalised net income of almost € 78 MM. At the same time, we have managed to consolidate our business model and generate value for our shareholders, patients, healthcare and pharmaceutical experts, employees and society."

## Message from the President

Dear shareholders,

As is the custom every year, I am addressing you to share and take stock of the achievements Almirall accomplished in the last business year. It was as complex as we had forecast, but proved to be a period in which we were able to lay the foundations for continued growth.

The effects of the spending cuts on health over the past three years in Spain have resulted in a 35 % drop in the volume of pharmaceutical sales, which have now fallen back to figures similar to those of 2003. In 2012, the impact of the increase in copayments was widely felt, whose effects will also carry over into 2013. Drugs sold at the price of generic products accounted for 67 % of the units sold and 40 % of values.

At Almirall, we have worked to make up for this situation in Spain by expanding our international operations, which now account for 60 % of our total turnover and are growing at a rate of 5 % per annum. We believe that over the next few years we will perform well on international markets. We are particularly confident that we will manage to strengthen our position in Europe.

Many of the efforts made over the past decade came to fruition in 2012 with the approval of two drugs that will mark the start of a new stage in our business. In recent years, we have been paving the way for growth and have taken advantage of these unprecedented opportunities in the history of our company.

Regulatory bodies have approved the commercialisation of our proprietary R&D compound aclidinium, which is used in the treatment of chronic obstructive pulmonary disease (COPD). In Europe, it is now available in the United Kingdom, Germany, Spain, Norway, Denmark and Iceland under the brand name Eklira<sup>®</sup> Genuair<sup>®</sup>/Bretaris<sup>®</sup> Genuair<sup>®</sup>, whilst in chemists in the United States it is sold as Tudorza<sup>TM</sup> Pressair<sup>TM</sup>.

Furthermore, the European Medicines Agency (EMA) gave the green light for linaclotide (Constella®), an innovative treatment for irritable bowel syndrome with constipation (IBS-c), whose launch has been planned for the first semester of 2013.

We are also making progress in breaking into new markets with Sativex<sup>®</sup>, a novel treatment for muscular rigidity (spasticity) caused by multiple sclerosis. In 2013, we hope to be able to start marketing it in five new countries in Europe, which will join Germany, Spain, Denmark and Norway where it is already available.

On the basis of the above comments, I am able to comment that in business terms the performance for the year was extremely positive. Despite the adverse global economic climate and Spain's continual austerity measures and cutbacks in public health spending, I believe that at Almirall we are on the right track to go on rising to the challenges of the 21<sup>st</sup> century, thanks to our innovation and international expansion.

Resolution and determination are needed to believe in innovation and investment in R&D, and at Almirall we do so and will continue to do so out of a deep-seated conviction. In 2012, we devoted around € 160 MM for R&D, which is over 23 % of our sales turnover.

These figures place Almirall as the pharmaceutical company that invests the most in R&D in Spain and ranks it third out of all the sectors in the country. This commitment to research, which began over 40 years ago, translates as an extremely strong team, which now numbers over 500 people.

Differentiation is the key to becoming a leader and managing change effectively. Almirall has done precisely that by establishing four priority therapeutic areas that make up our current growth platforms: respiratory, dermatology, gastrointestinal and pain. We have also strengthened our trading agreements with third parties in order to make our drugs available to as many patients as possible.

We have consolidated our international presence through 14 affiliates, following the addition of a new organisation in Canada that will help us to increase our visibility in foreign markets.

Courage, leadership and commitment have led our management strategy in 2012. This helped boost our total revenues to over  $\in$  900 MM and generated a normalised net income of almost  $\in$  78 MM. At the same time, we have managed to consolidate our business model and generate value for our shareholders, patients, healthcare and pharmaceutical experts, employees and society.

Therefore, I am pleased to announce that we will table a proposal at the AGM to pay out a dividend of  $\in$  0.15 gross per share (rounded figure), either in cash or as scrip dividend shares.

The Board of Directors also saw changes with the addition of two experts from the pharmaceutical industry who have long-standing international experience: Gerhard Mayr and Karin Dorrepaal. Another change was the appointment of new members to the Audit Committee, which reviews the periodic financial statements and monitors compliance with all legal requirements and the proper application of accounting principles. Juan Arena was appointed as chairman of the Audit Committee for the second time in May 2012 and Gerhard Mayr was voted in as a member, a post he took up on 1 January 2013.

Also worthy of special mention is the approval of the Code of Ethics, which comes into effect in 2013. It is intended to serve as a guideline for all of Almirall's employees by setting them high standards of conduct at the workplace.

Share price performance in 2012 was excellent, with a revaluation of over 40 %, compared to -5 % of the IBEX 35. There was also a clear upward trend in the first weeks of 2013.

In a highly competitive and demanding environment, we set ourselves new challenges and planned key launches for 2013. Each and every one of the almost 3,000 professionals who belong to Almirall is aware that the health sector is a top priority in every country and that companies like ours contribute to improving the quality of life of people. Therefore, to conclude my overview of such an eventful year, I would like to thank all of our employees for their hard work and to endorse the following message: at Almirall, the best is yet to come. We hope to continue to warrant your trust.

Yours sincerely,

Jorge Gallardo Ballart President



"To conclude my overview of such an eventful year, I would like to thank all of our employees for their hard work and endorse the following message: at Almirall, the best is yet to come."



Eduardo Sanchiz *CEO* 

"It was a landmark year for Almirall as the major regulatory milestones and collaboration agreements reached enabled us to set the pace for a new period of growth in the medium and long-term, and we also met our financial targets."

## Interview with the CEO

#### How would you rate performance in 2012?

Very positively indeed. It was a landmark year for Almirall as the major regulatory milestones and collaboration agreements reached enabled us to set the pace for a new period of growth in the medium and long-term, and we also met our financial targets.

We attained these goals in an increasingly complex environment by remaining true to our strategic direction, based on innovation and global outreach, maintaining our leading position in our key therapeutic areas and continuing to make our high added value treatments available to society.

#### What would you highlight in particular?

Our challenges included strengthening our future growth platforms and continuing to promote internationalisation. We successfully rose to these challenges and laid the foundations for future growth by doing so.

With regard to the respiratory area, in July the regulatory agencies in the United States (FDA) and Europe (EMA) approved the commercialisation of aclidinium, which is prescribed as a treatment for relieving the symptoms of chronic obstructive pulmonary disease (COPD) in adult patients. As far as the gastrointestinal area is concerned, in November the EMA authorised the use of linaclotide in the treatment of irritable bowel syndrome with constipation (IBS-c). This was the first drug approved by the EMA to treat this disorder, which is estimated to affect almost 4 % of the adult population in Europe.

In addition to the advances made in the respiratory and gastrointestinal areas, it is worth highlighting the dermatology area, which now accounts for almost 20 % of our total business and grew by 8 %. We continue to be leaders in prescription drugs in Germany and we are now ranked 7<sup>th</sup> in Europe. This is without a doubt one of our future growth platforms.

Furthermore, following the opening of our new affiliate in Canada, we now have a total of 14 affiliates, which means we have sales capabilities in 22 countries spread across Europe and North America. Almirall continued to expand its global presence, as reflected by the fact that 60 % of our total turnover came from our international operations, which we expect to grow once again in 2013.

# What other aspects do you think were of particular interest in the area of corporate development?

This was another key line of action in 2012 for bringing about future growth. Our plan is to promote partnerships with other companies that will make us very competitive in our different markets and, therefore, to realise the full potential of our new products, especially aclidinium. We have established trading alliances with the Menarini Group in a number of countries in Europe, as well as in Australia and New Zealand. Further alliances included development and marketing agreements with Daewoong in Korea, and with Forest for the Canadian market. As a result of these agreements, plus the ones already in place, 90 % of the aclidinium global market is directly or indirectly covered by us.

In Spain we reached an agreement with Bayer for the co-promotion of Xarelto<sup>®</sup> (rivaroxaban), a novel cardiovascular drug that shows great promise in the treatment of atrial fibrillation.

#### How would you assess the results in 2012 from an economic and financial point of view?

In 2012, we increased our total revenues by 3 % to reach a figure of over  $\in$  900 MM, whilst net sales decreased by 11 %, as had been forecast, due to the austerity measures implemented in Spain over the past three years. However, I should once again like to point out that our international sales grew by 5 % and now account for 60 % of our total turnover.

In terms of net income, we made  $\in$  76 MM and the net normalised income was in the region of  $\in$  78 MM, as anticipated. This was due to two main reasons: increased spending on R&D in order to build up our respiratory franchise, and additional operating expenses following the expansion of our affiliates and the launch of new products, especially aclidinium.

These results are in line with the financial indicators that we released at the beginning of the year to our investors. There were therefore no surprises.

On a financial level, we closed the year with a very healthy balance sheet following the cancellation of all of our debt, with a positive cash flow position of  $\in$  52 MM and a balance sheet position whereby the shareholders equity accounted for 68 % of total assets.

#### What progress is being made in Almirall's R&D portfolio?

In R&D, for which we devoted 23 % of our sales in 2012, we have made significant progress in our key therapeutic areas, namely, respiratory, dermatology, gastrointestinal and pain. We have three relevant projects currently in phase III, which is the last phase in clinical development, out of a total of 6 projects in the clinical development phase. The first is the combination of aclidinium with formoterol, which we hope will be added to our COPD franchise in the near future. We are also continuing to make advances with the new indication of Sativex<sup>®</sup> as a treatment for cancer pain, and we have a relevant opportunity in dermatology using LAS41008 for the treatment of psoriasis.

#### What is the outlook for Almirall in 2013?

We are taking an optimistic attitude, despite the extremely difficult economic environment in the health sector. At the end of last year we launched aclidinium in Germany, the United Kingdom and a number of Nordic Countries, as well as in the United States, and we began 2013 by introducing the product in Spain.

In the first half of 2013, we also plan to make linaclotide available to patients and healthcare professionals. Both are pillars of growth that, together with our dermatology franchise and Sativex<sup>®</sup>, contribute to the growth of the company's sales.

Together with our trading partners, we have planned over 30 product launches in 2013 for our three main products. It will therefore be a year in which we will place a great deal of emphasis on executing our strategy, which will go hand in hand with a heavy investment in product launches so that our new products realise their full potential.

In 2013, we will continue to pursue corporate development opportunities through new licences on executing our key therapeutic areas or selective acquisitions, whilst keeping our main focus on our number one priority: the launch of new products in different countries.

#### What message would you like to send out to shareholders?

That they should continue to place their full trust in the company. Share price performance in 2012 was excellent, with a revaluation of over 40 % compared to -5 % of the IBEX 35. There was also a clear upward trend in the first weeks of 2013. As I pointed out earlier, in 2012 we laid the foundations for sustained growth in the medium to long-term. We have the catalogue of products, the internal alignment and the ability to do so. Our ultimate aim is to generate value for our shareholders that reflects the growth of our business. The work, enthusiasm and commitment of the almost 3,000 professionals who belong to Almirall will ensure this goal is met.

"In 2012 we laid the foundations for sustained growth in the medium to long-term. We have the catalogue of products, the internal alignment and the ability to do so. Our ultimate aim is to generate value for our shareholders that reflects the growth of our business. The work, enthusiasm and commitment of the almost 3,000 professionals who belong to Almirall will ensure this goal is met."

## 2012 highlights

# January

## 25

Alliance with BioFocus, a subsidiary of Galapagos NV, to conduct research in the area of respiratory diseases.



# February

## 2

Almirall's affiliate in Mexico celebrates its 10<sup>th</sup> anniversary. Over the last three years, it has launched nine products for the treatment of gastrointestinal and dermatological diseases.

## 13

Agreement with the Korean firm Daewoong Pharmaceuticals for aclidinium, used in the treatment of chronic obstructive pulmonary disease (COPD).

## 29

Two research grants awarded for the study of muscular rigidity in multiple sclerosis (MS).

# March

## 15

Commercial rights obtained in Mexico to sell Sativex<sup>®</sup>, used in the treatment of muscular rigidity in multiple sclerosis (MS).



## 26

Partnership with the Menarini Group for aclidinium in the EU, except for the United Kingdom, the Netherlands and the Nordic Countries, where Almirall has exclusivity rights.

# Second quarter

# May

## 4

Approval at the AGM of a scrip dividend of  $\in$  0.18 gross per share, redeemable in cash or as fully paid-up newly issued shares.



## 24

Cession of the rights on the second generation inhibitor for rheumatoid arthritis (LAS186323) to Aslan Pharmaceuticals.

# June

## 6

Abediterol, a long-acting beta-agonist (LABA) developed by Almirall, obtains better results in COPD patients (phase Ila studies) than indacaterol.

## 8

The new shares issued as a way of remunerating shareholders become listed.



# July

20

The European Medicines Agency (EMA) approves aclidinium in all countries in the European Union, Iceland and Norway.



24

America's health authorities (FDA) authorises the commercialisation of aclidinium, used to treat COPD in the USA.

# September

## 5

Almirall extends its an affiliate with the opening of an affiliate in Canada.

## 7

Almirall acquires the commercialisation rights on linaclotide, used in the treatment of irritable bowel syndrome with constipation (IBS-c), in Mexico.

## 20

First sales of aclidinium in Denmark, followed by Germany and the United Kingdom, under the trademark Eklira® Genuair®.

# ourth quarte

# October

## 10

Cession of the commercial rights on aclidinium for Australia and New Zealand to Invida, part of the Menarini Group.

## 22

Gerhard Mayr appointed as an independent external director at Almirall.

## 23

Almirall becomes a shareholder of the Spanish biotechnology company AB-Biotics in order to fund genetics research projects.

# November

## 19

Karin Louise Dorrepaal appointed as an independent external director at Almirall, a post she took up on 1 January 2013.



28

The EMA authorises the commercialisation of linaclotide for the treatment of IBS-c in Europe under the brand name Constella<sup>®</sup>.

## December

15

Sales of aclidinium start in the United States under the brand name Tudorza™ Pressair™.





# ABOUT US

Almirall is a pharmaceutical company committed to health that bases its strategy on innovation and international growth. Its work benefits thousands of healthcare professionals and millions of patients all over the world.

• **18** Mission, vision and strategic direction • **19** Corporate values

• 20 Business model • 21 Stakeholders • 22 Corporate governance

## Mission, vision and strategic direction

Almirall is a pharmaceutical company committed to health that bases its strategy on innovation and international growth. Headquartered in Barcelona (Spain), Almirall researches, develops, manufactures and markets proprietary R&D and third party drugs for the purpose of improving people's health and well-being.

## Mission and vision

In 2012 we redefined our mission and vision in order to be able to give greater value to the company and to better adapt to the changing demands in the field of health and in the general environment.

## **Mission**

Provide valuable medicines to you and future generations.

## Vision

Be recognised as an innovative pharmaceutical company situated among the top players in our strategic therapeutic areas with a strong European presence and global reach.

## Strategic direction

Almirall concentrates all of its efforts and resources on:

- Seeking innovative medicines through our own R&D and with external partnerships, licenses, acquisitions and collaborations.
- Becoming a relevant player in respiratory and dermatology with a strong interest in gastroenterology and pain.
- Expanding our direct presence and critical mass internationally while maintaining a leading position in Spain.
- Addressing evolving customer needs and improving patient outcomes.





- 1. Headquarters (Barcelona, Spain).
- 2. The Genuair<sup>®</sup> inhaler developed at the Centre of Excellence for Inhalation (Bad Homburg, Germany).

## **Corporate values**

Almirall's corporate values define our culture: the way we work and the way in which we interact on a professional and personal level, both inside and outside the organisation.

Our values help to set us apart from our competitors, establish the guidelines we follow for channelling the organisation's collective efforts and enable us to better put our position across to our various internal and external stakeholders.

At Almirall we are aware that the four values that define us as a company add up and help us to boost our performance and generate value. Our overall results are the sum total of individual efforts devoted to fulfilling our vision, targets and goals.

## **Corporate values**

- Trust
- Innovation
- Partnership
- Personal accountability





- 3. Almirall drugs.
- 4. Almirall's R&D in Sant Feliu de Llobregat (Barcelona, Spain).

## **Business model**

The main feature of our portfolio of drugs is that it includes a balanced proportion of branded medicines comprising R&D proprietary products and products licensed by third parties, as well as a greater diversification of products, therapeutic areas and geographical areas. Almirall's catalogue of treatments is sold through its 14 affiliates in Europe, Mexico and Canada, and through agreements with trading partners in over 70 countries on the five continents.



## **Stakeholders**

As a result of its daily business dealings, Almirall maintains a smooth relationship with its stakeholders, who are basically involved in the fields of research and healthcare. This relationship is kept alive through a number of tools adapted to each stakeholder.

## Patients

We strive to provide treatments that improve patients' health and quality of life. We make innovative drugs that satisfy needs as yet uncovered in the respiratory area, in which we are most noted for our work to mitigate the effects of chronic obstructive pulmonar disease, as well as for spreading a greater understanding and social awareness of little known pathologies that come at a high personal cost, such as irritable bowel disease with constipation.

#### Healthcare professionals

At Almirall we interact with this community in order to ascertain its demands and needs, as well as to provide it with the latest information about our products, mainly doctors and pharmacists. To do so, we arrange meetings to promote cooperation with healthcare professionals. We also keep communication channels open with academic institutions, hospitals and scientific societies with the aim of fostering joint programmes and projects that contribute to improving health.

## Employees

At the company we are both keen to retain talent and recruit new professionals who enrich our staff. We encourage that the working environment is a place where our staff can develop professionally and personally. We therefore encourage them to engage in continuous training and we closely monitor compliance with regulations on occupational hazard prevention and other areas.

#### Shareholders, investors and financial institutions

We nurture this group of stakeholders by being transparent with them and keeping them informed. True to our values of integrity and credibility, financial transparency is one of our overriding goals.

#### Strategic partners

At Almirall, we believe that working with other companies in the sector is a way of growing that also enables us to offer a balanced, highly competitive portfolio of products, as well as to strengthen the internationalisation of our business. These strategic alliances cover the whole of the medicine value chain.

#### Non-governmental organisations

We work with a number of not-for-profit organisations in order to promote activities, provide services and fund projects that we consider fundamental to the social development of the most underprivileged people and regions.

#### Health authorities and associations

Almirall complies with all legal and administrative processes required of it by the health authorities in all of the business it conducts. Furthermore, as a pharmaceutical company, it works alongside associations in the sector in developing projects related to health. Amongst others, Almirall is a member of the European Federation of Pharmaceutical Industries & Associations (EFPIA) and the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA).

#### Media

Our interaction with media is an important part of our business. At Almirall we cooperate and are transparent with all of the media that wish to know about, understand and publish information on our business.

### **Suppliers**

All of Almirall's suppliers must satisfy a number of criteria that are in line with our social commitment. Therefore, we give priority to suppliers that have quality (ISO 9001), environmental (ISO 14001), and occupational health and safety (OHSAS 18001) certificates.

## Corporate governance

The fundamental purpose of Almirall's corporate governance policy is to protect the interests of over 30,000 shareholders worldwide. It is considered a key tool for ensuring the transparency and integrity of all information published by the company.

Five bodies are responsible for Almirall's Corporate governance. They each have clearly defined functions that are regularly reviewed to ensure they meet their goals to the best of their ability. These bodies and their functions are as follows:

- The Board of Directors, whose main goal is to defend the interests of shareholders, transparency and the integrity of information.
- The Audit Committee, which is responsible for conducting reviews of the periodic financial information reported and for ensuring compliance with all legal requirements and the proper application of accounting standards. It also monitors internal auditing systems, internal controls and risk management practices, in addition to liaising with the external auditor.
- The Appointments and Remuneration Committee, which monitors the selection process and remuneration policy of the company's directors and senior management.
- The Corporate Compliance Committee, whose mission is to support and monitor the implementation and compliance of our occupational hazard prevention management system.
- The Management Board, whose function is to define the company's general strategy and its specific application to R&D, business operations, finance and corporate development.

Amongst other projects undertaken and approved in 2012 by the various corporate governance bodies, it is worth highlighting Almirall's new Code of Ethics, which contains the company's basic principles of behaviour and conduct based on internal guidelines and the applicable regulations.

In 2012, Almirall had over 30,000 shareholders. Their interests are safeguarded by the Board of Directors, whose proposals must ultimately be approved at the Annual General Meeting. In order to uphold the integrity and independence of these proposals, the Audit Committee and the Appointments and Remuneration Committee play an active, major role in drawing them up.

## Management Board

Defines the company's general strategy.

## Audit Committee

Reviews the periodic financial information reported and ensures compliance with all legal requirements and the proper application of accounting standards.

About us

## Corporate Compliance Committee

Supports and monitors the implementation and compliance of our occupational hazard prevention system.

> Transparency and integrity in defending the interests of over 30,000 shareholders

## Board of Directors

Defends the interests of shareholders, transparency and the integrity of information.

## Appointments and Remuneration Committee

Monitors the selection process and the remuneration policy of the company's directors and senior management.

## **Board of Directors**

In 2012, Almirall's Board of Directors was joined by new members to make a total number of ten directors, following the approval of these appointments by the AGM. The first of these appointments was that of Gerhard Mayr, who was appointed as an independent external director.

The second of these appointments was that of Karin Louise Dorrepaal, who was voted in by co-option. She was also made an independent external director, a post that she was to take up on 1 January 2013.



#### **BOARD OF DIRECTORS**

As at 31 December 2012

President	Jorge Gallardo Ballart	Director
1 <sup>st</sup> Deputy President	Antonio Gallardo Ballart	External director
2 <sup>nd</sup> Deputy President	Daniel Bravo Andreu	External director
Member	Juan Arena de la Mora	Independent external director
Member	Paul Brons*	Independent external director
Member	Tom McKillop	Independent external director
Member	Gerhard Mayr	Independent external director
Secretary (Non-member)	José Juan Pintó Sala	Non-director
Member	Eduardo Sanchiz Yrazu	Executive director
Member	Luciano Conde Conde	Executive director
Member	Bertil Lindmark	Executive director

\*On 1 January 2013, Karin Louise Dorrepaal, appointed by co-option in November 2012, replaced Paul Brons as an independent external director.



## MEMBERS OF THE BOARD IN 2013:

## 1 Jorge Gallardo Ballart

President and director

PhD in Industrial Engineering

Institutional positions at the EFPIA and Farmaindustria over several periods

Member of Spain's Royal Academy of Pharmacy and awarded the President Macià Medal for services rendered

## 2 Antonio Gallardo Ballart

1st Deputy President and external director Further studies in commerce and business management Awarded the plaque of the Civil Order of Public Health and the Medal of Merit for services rendered

#### 3 Daniel Bravo Andreu

2<sup>nd</sup> Deputy President and external director Degree in Pharmacy

Partner and member of the Board of Directors in several companies

#### 4 Juan Arena de la Mora

### Member and independent external director PhD in Electromechanical Engineering and MBA Member of the Board of Directors in various companies and holder of the Great Cross of Civil Merit

#### 5 Tom McKillop

#### Member and independent external director PhD in Chemistry

Institutional positions in the EFPIA and other organisations Several civil awards as a member of the Academy of Medical Sciences and honorary member of the Royal Society of Chemistry. Knighted in 2002

#### 6 Gerhard Mayr

#### Member and independent external director

Chemical engineer

Has held positions in several companies in the

pharmaceutical sector

President and member of the Board of Directors of several companies

#### 7 Karin Louise Dorrepaal

Member and independent external director Doctor of medicine and MBA Has held positions in several companies in the pharmaceutical sector

#### 8 José Juan Pintó Sala

## Secretary (Non-member) Degree in Law Practises in various law firms and member of the Bar Associations of Barcelona and Madrid

## 9 Eduardo Sanchiz Yrazu

Member and executive director Degree in Economics and MBA Has held positions in several companies in the pharmaceutical sector Current Chief Executive Officer at Almirall

## 10 Luciano Conde Conde

Member and executive director Degree in Pharmacy and Master's Degree in Business Management and Marketing Has held positions in several companies in the pharmaceutical industry Current Chief Operating Officer at Almirall

## 11 Bertil Lindmark

#### Member and executive director

Degree in Medicine and PhD in Molecular Epidemiology Has held positions in several companies in the pharmaceutical industry Current Chief Scientific Officer at Almirall

## Audit Committee

The company has an internal audit function and an annual external audit process that guarantees the integrity of the financial information reported.

The Audit Committee meets once every quarter to review the periodic financial information that is to be submitted to the Stock Exchange authorities, as well as the information that will be approved by the Board of Directors and included within the annual filings.

The Board's Regulations also establish that the Committee may meet at the request of any of its members or every time a meeting is called by the Chairman, who is required to call a meeting whenever the Committee or its Chairman requests the issue of a report or the adoption of proposals, and, in any event, whenever deemed necessary for the proper discharge of its functions.

In 2012, the appointment of Gerhard Mayr as a member of the Audit Commitee can be highlighted. A chemical engineer with longstanding experience in companies in the pharmaceutical sector, he took up his post on 1 January 2013 to replace Paul Brons.

The table below shows the members of the Committee as at 31 December 2012.

## AUDIT COMMITTEE

Chairman	Juan Arena de la Mora
Member	Daniel Bravo Andreu
Member	Paul Brons*

\*Gerhard Mayr took over as a member of the Audit Committee from Paul Brons on 1 January 2013.

## Appointments and Remuneration Committee

This Committee meets once every quarter and must also do so every time a meeting is called by the Chairman, whenever the Board or its Chairman requests the issue of a report or the adoption of proposals, and, in all cases, whenever deemed appropriate for the proper discharge of its functions. It reports on its activities to the first plenary meeting of the Board of Directors following its own meetings. Furthermore, the Committee must take minutes of its meetings, of which a copy must be sent to every member of the Board. Whenever deemed necessary to discharge its functions adequately, the Committee may also seek advice from external experts. The table below shows the members of the Committee as at 31 December 2012.

#### APPOINTMENTS AND REMUNERATION COMMITTEE

Chairman	Tom McKillop	
Member	Antonio Gallardo Ballart	
Member	Jorge Gallardo Ballart	

## **Corporate Compliance Committee**

Almirall has a compliance policy that applies to all areas of the company for the purpose of providing the organisation with a system for monitoring legal risks. Its fundamental goal is to check compliance with regulations (legal, contractual and internal) to which Almirall is subject, as well as to control the potential liabilities of the company and/ or its directors, board members and legal representatives as a consequence of breaching regulations.

The Compliance Committee is the body responsible for supporting and monitoring the implementation and compliance of legal regulations. It is made up of the President of the company, the CEO, the Chief Operating Officer, the Chief Scientific Officer, the Chief Financial Officer, the Corporate Director of Human Resources, the Director of Internal Audit and the General Counsel. The purpose of the Committee is to review reports on legal risks and, if necessary, approve the implementation of the measures to be taken to remedy them.

## Management Board

This is the company's leading governing body on which Almirall's main organisational areas are represented.

The Management Board is made up of eight members. It is chaired by the CEO, a position held by Eduardo Sanchiz since 2011.



## **MANAGEMENT BOARD**

As at 31 December 2012

1 Chief Executive Officer	Eduardo Sanchiz Yrazu
2 Executive Director, Chief Operating Officer	Luciano Conde Conde
3 Executive Director, Chief Scientific Officer	Bertil Lindmark
4 Corporate Director, Chief Financial Officer	Daniel Martínez Carretero
5 Corporate Director, Human Resources	Javier Arroniz Morera de la Vall
6 Corporate Director, General Manager Spain	Enrique Domínguez Cruz
7 Senior Director, Industrial Area	Eloi Crespo Cervera
8 Senior Director, General Counsel & Secretary to the Management Board	Joan Figueras Carreras





# BUSINESS PERFORMANCE IN 2012

Last year was a landmark year for Almirall. It marked a turning point in establishing the conditions for sustained growth in the mid to long-term. We remained true to our strategic direction, based on innovation and international growth.

30 Highlights in R&D • 31 Strategic therapeutic areas • 36 Pipeline
37 Patents • 38 R&D centres • 39 R&D partnerships • 40 Global reach of Almirall's drugs • 42 Growth platforms • 46 OTC products • 48 Corporate development agreements • 50 Business year sales • 53 Production

## Highlights in R&D

Research has formed part of Almirall's DNA for over 40 years, as reflected by our commitment to the development of new drugs that will help treat illnesses in the future.

**20%** of staff devoted to R&D

**23%** of sales invested in R&D

**59%** of sales come from proprietary drugs

In 2012, Almirall reinvested over 23 % of its sales in R&D – an increase of 10 % on the previous year. These figures make it the pharmaceutical company that invests the most in R&D funding in Spain and ranks it third out of all sectors in the country. On a European level, we are ranked  $13^{\rm th}$  in terms of investment in R&D.

This firm commitment to R&D allowed us to make 59 % of our sales from proprietary drugs.

The human resources devoted to R&D accounted for 20 % of our staff by the end of 2012. The 500-plus scientists and experts at Almirall play an essential role in all product phases, from the research and development process to registration applications to authorise their commercialisation.

## In 2012, aclidinium and linaclotide became approved therapeutic solutions

## **Milestones in 2012**

- The regulatory bodies in the United States (FDA) and Europe (EMA) approved the sale of our compound, **aclidinium**, used for the treatment of chronic obstructive pulmonary disease (COPD).
- The European Medicines Agency also gave the green light to **linaclotide**, a first-in-class treatment for irritable bowel syndrome with constipation (IBS-c).
- We have three development projects in phase III. The first is the **combination of aclidinium with formoterol**. Clinical trials are also in progress for a new use of **Sativex®** to relieve cancer pain. Finally, **LAS41008** for treating psoriasis.







## Strategic therapeutic areas

One of Almirall's priorities is to promote proprietary R&D focused on four strategic therapeutic areas for the company.

## Key therapeutic area: respiratory

Asthma and COPD, the respiratory diseases on which Almirall concentrates its efforts, are extremely prevalent and have a substantial overall impact in terms of morbidity, mortality, decline in quality of life and cost to society.

#### Asthma

Asthma is an inflammatory condition of the respiratory tract and one of the most common chronic conditions. WHO estimated that it affected over 200 million people around the world and is most common during childhood. There are still unmet needs in this indication. These include improving the posology and format of the drugs to make them easier for patients to take and use, as well as developing new, more effective and safer non-steroidal treatments.

#### • Chronic obstructive pulmonary disease (COPD)

COPD is a progressive illness that is often potentially fatal. It triggers an abnormal inflammatory response of the lungs to noxious particles or gases, which results in the obstruction of the airways that is not totally reversible. WHO estimated that it affected over 300 million people worldwide suffer from COPD and that between 200,000 and 300,000 people die of this disease\* in Europe every year. These figures could increase by more than 30 % over the next 10 years if the risks are not reduced, particularly exposure to tobacco smoke.

Treatments target controlling the symptoms and slowing down the progression of the illness, depending on the stage it has reached (mild, moderate, severe or very severe), which is diagnosed on the basis of pulmonary function tests (spirometry) and the symptoms shown by patients. Patients with mild symptoms are treated with short-acting bronchodilators (SAMA, SABA), and as symptoms advance into the moderate-severe stages long-acting bronchodilators (LAMA, LABA) are added to the treatment. LAMAs are the cornerstone for treating COPD and are recommended for all groups of patients.

SAMA: short-acting muscarinic antagonist SABA: short-acting B2-agonist LAMA: long-acting muscarinic antagonist LABA: long-acting B2-agonist Cabal Initiative Corporation Obstructive Lung Disea

\* Global Initiative for Chronic Obstructive Lung Disease 2011.

Currently, aclidinium monotherapy (a proprietary LAMA compound administered using the Genuair<sup>®</sup> inhaler) is a treatment that has been readily available to COPD patients since its approval by the regulatory bodies in Europe and the United States in 2012.

"COPD significantly affects the quality of life of patients and puts a huge burden on their families and carers. The introduction of new effective, well-tolerated treatments that contribute to alleviating the daily exacerbations of people suffering from breathlessness is always welcome news. The green/red display windows on the Genuair® inhalers will help improve the way they are used, which will have beneficial repercussions on COPD patients and their carers."

#### Professor Paul Jones

Professor of Respiratory Medicine and Head of the Division of Clinical Science at St George's, University of London.



#### 2012 Almirall Annual Report

# Respiratory franchise. Advances made in development projects in 2012

Our projects in development focus on combinations of long-acting bronchodilators (LAMA/LABA) and inhaled corticosteroids (ICS). All compounds used in studies are administered using our Genuair<sup>®</sup> inhaler.



## • Combination of aclidinium and formoterol

Two pivotal, double blind phase III studies with the two compounds in fixed dose combination are in progress.

- Long-term efficacy and safety study (NCT01462942) This study is being conducted in Europe, South Africa and South Korea on a total of 1,575 patients. It aims to assess the long-term efficacy and safety of a fixed dose combination of aclidinium bromide and formoterol fumarate.
- Long-term efficacy and safety study (NCT01437397) This study is being conducted in the United States, Canada, Australia and New Zealand on a total of 1,550 patients. It aims to assess the long-term efficacy, safety and tolerance of a fixed dose combination of aclidinium bromide and formoterol fumarate.

#### • Fixed dose combination of abediterol

Abediterol is an inhaled long-acting beta-antagonist (LABA) that is taken once daily. In the phase II studies performed on asthma sufferers, it proved to be fastand long-acting (24 hours).

# • Results of the phase IIa studies on patients with COPD

The results of a phase lla study using single doses on patients with COPD were published in 2012. They showed that administering abediterol in once-a-day doses had a potentially greater bronchodilatory effect than indacaterol, the only once daily LABA currently available on the market. Abediterol was administered using Almirall's multidose dry-powder Genuair® inhaler.

#### • MABA

The clinical candidate has been identified and will enter phase I during 2013. This could be the first step towards a triple combination.

## Key therapeutic area: dermatology

The research into dermatology focuses on improving the quality of life of patients with inflammatory skin conditions, such as psoriasis and eczema. Although skin diseases are not usually life threatening for sufferers, they can have a profound effect on their social and working lives.

#### • Psoriasis

Psoriasis is a chronic inflammatory disease that manifests itself as scaly, swollen lesions, and can be the first stage of skin cancer. WHO estimated that between 1 and 3 % of the world population suffers from this non-contagious disease that can affect any part of the skin.

#### • Eczema

Eczema is a skin condition characterised by rashes that can give rise to such manifestations such as redness, blistering, crusting, and oozing. The characteristic redness of affected areas of the body is accompanied by severe itchiness. It can easily spread quickly to other parts of the body.

# Dermatology franchise. Advances made in development projects in 2012

In 2012, two phase III studies for psoriasis were in progress and a third project for the treatment of skin inflammation was submitted for registration.

• Emulsion for the treatment of inflammatory skin conditions (LAS41002)

Filed for registration in 2012, this emulsion is used for the treatment of inflammatory skin conditions, such as psoriasis and eczema.

• Topical treatment for psoriasis (LAS41004) This proprietary topical treatment for psoriasis is currently in clinical phase II, whose aim is to ascertain its efficacy as an anti-inflammatory skin cream.

• Oral treatment for psoriasis (LAS41008) Phase II was completed in 2012 and this oral treatment entered a clinical phase III programme to generate pivotal data on the efficacy and safety of this R&D compound. Results are expected in 2014.



Skin diseases can have a profound effect on the social and working lives of patients

## Key therapeutic area: gastrointestinal

The main project in this area focuses on irritable bowel syndrome (IBS). This is a multifactorial disease that is generally a result of the interaction of three principal traits: psychosocial, changes in gastrointestinal motility, and increased sensitivity in the colon or bowel, which is associated with symptoms of pain and discomfort.

The estimated prevalence of IBS is between 10 and 15 % of the population in Europe and the United States; this puts it on a par with better known conditions such as migraine and asthma\*.

Current treatments for IBS focus on individual symptoms, but there is a need for effective, well tolerated treatments. IBS is classified into IBS with constipation (IBS-c), IBS with diarrhoea (IBS-d) and IBS of a mixed type (IBS-m).

Approximately one third of patients with IBS are chronic sufferers with abdominal pains and swelling, and constipation. They are diagnosed as having irritable bowel syndrome with constipation (IBS-c).

# Projects under development. Irritable bowel syndrome with constipation (IBS-c)

Irritable bowel syndrome (IBS) is a chronic, functional, disorder that causes abdominal pain and discomfort associated with constipation and swelling.

In 2012, the European Medicines Agency (EMA) approved Marketing Authorisation of linaclotide for patients suffering from IBS-c and is now available to them as a treatment.

Constella® (linaclotide) is a first-in-class compound licensed from Ironwood Pharmaceuticals for Europe.

A number of studies conducted have demonstrated that linaclotide alleviates abdominal pain and swelling as well as regulating gastrointestinal motility, thus increasing the number of bowel movements.



"Although it affects over 10 % of the population in the EU, there are few effective alternatives for treating IBS. Approximately one third of patients with IBS suffer from type IBS-c and the approval of linaclotide has provided doctors with an innovative drug able to improve the life of patients whose quality of life is impaired."

#### Professor Jan Tack

Head of the Department of Gastroenterology and Professor of Internal Medicine at the Gasthuisberg University Hospital at the University of Leuven, Belgium.

\* P.S. Hungin et al. The prevalence, patterns and impact of irritable bowel syndrome: an international survey of 40,000 subjects- Aliment Pharmacol Ther 2003;17:643-650 Almirall develops first-in-class compounds with various strategic partners

## Key therapeutic area: pain

Cancer and its treatment can sometimes cause moderate to severe pain. There are a number of biological reasons why cancer sufferers feel pain, including: the effect of surgery, radiation treatment and/or chemotherapy; the healing of scars following treatment; and the spread of a tumour to other organs, nerves or other parts of the body.

#### Projects under development. Cancer pain

The drug, Sativex<sup>®</sup> (CBD:THC), is already available as a first-in-class treatment for spasticity or muscular rigidity caused by multiple sclerosis (MS). Sativex<sup>®</sup>, which was licensed from GW Pharmaceuticals, is currently undergoing studies for use in the treatment of cancer pain.

Specifically, it is an endocannabinoid system modulator designed to optimise therapeutic efficacy and minimise psychotropic side effects based on the combination of two cannabinoids in equal proportion (CBD: cannabidiol and THC: delta-9-tetrahydrocannabinol).

Phase II was successfully completed with 500 patients in 2010 and phase III studies began in the United States and Europe. Results are expected in 2014.

## Successful partnerships in the development of pioneering drugs

Almirall has wide experience in partnerships with other companies to develop innovative drugs, including first-in-class treatments. This experience places Almirall as a leading partner for other companies as it is able to contribute its knowledge and resources, from the first stages of development to the registration and subsequent commercialisation. Sativex<sup>®</sup> and linaclotide are two cases in point of Almirall's commitment to providing real solutions for specific illnesses.


# **Pipeline**



# All of our clinical studies are in strict compliance with criteria of transparency.

At Almirall we provide reliable and transparent information about our drugs and development projects. All of our clinical studies are therefore posted on <u>www.clinicaltrials.gov</u> and on our website, as recommended in the EFPIA guidelines: Joint Position on the Disclosure of Clinical Trial Information via Clinical trial Registries and Databases. Our clinical studies are conducted in line with the regulations of the countries in which they are performed and pursuant to the following international guidelines and agreements: the Declaration of Helsinki, which protects the rights of participants in clinical studies; the Good Clinical Practice (GCP) standards, which are a set of procedures and regulations to ensure the safety of participants and the guidelines of the International Conference for Harmonisation (ICH), which were drawn up by representatives from the health authorities in Europe, the USA and Japan, and from the pharmaceutical industry.

## Patents

In 2012, Almirall has actively pursued the policy protection of its intellectual property, as reflected in the submission of applications for 16 new inventions. At the end of 2012, Almirall had 81 active patent families, which corresponded to a total of 1,118 successfully filed patents and 1,031 applications awaiting approval in 70 countries.

The company also has 886 umbrella brands, which protect over 5,000 brands worldwide and 1,400 domain names on the Internet. All of the drugs sold or in development in 2012 are protected by solid patent and brand portfolios.

### **Eklira® Genuair®, patent-status**

Our product Eklira<sup>®</sup> Genuair<sup>®</sup> (Tudorza<sup>™</sup> Pressair<sup>™</sup> in the USA) is protected by 14 patent families that cover different aspects of the product (chemical structures, formulations, new indications, combinations, etc.), as well as the inhaler.

Immediately after receiving Marketing Authorisation for aclidinium in the USA and the EU, all documentation necessary for acquiring a five-year patent term extension (PTE) on the basic patent was filed. This was the first patent filed by Almirall to protect the chemical structure of aclidinium. Once granted, this PTE (known in the EU as a Supplementary Protection Certificate) will extend the term of the patent until 2025. In addition, six of the patents that protect aclidinium appear in the FDA's Orange Book and other patents will also be included to it once approved by the USA's Patent and Trademark Office.

The portfolio of aclidinium patents will also protect its combination with formoterol, which is currently being developed. Almirall also has a patent that specifically protects this combination in the most relevant territories around the world.



## **R&D** centres

Almirall has three R&D centres, two in Spain and one in Germany. In addition, Almirall has an extensive collaboration networks with universities and other scientific institutions to support projects in development and promote the generation of new research programmes.

### **R&D** Centre of Excellence in Sant Feliu de Llobregat (Barcelona, Spain)

Almirall carries out most of its R&D activities in its facility located in Sant Feliu de Llobregat (just outside of Barcelona), which was inaugurated in 2006. This R&D centre, with a surface area of over 27,500 m<sup>2</sup>, is equipped with the most advanced technology and employs over 300 highly qualified professionals who

cover all the disciplines involved in the process of conducting the research and development of a new drug. In addition to this centre, Almirall also has a chemical plant in Sant Andreu de la Barca (also in the Barcelona area). It supplies the active ingredients needed for toxicological, pre-clinical and clinical studies.



### Almirall Centre of Excellence for Inhalation in Bad Homburg (Germany)

Located near Frankfurt, it was incorporated into Almirall's centres of excellence in 2006. It has a total surface area of 5,600 m<sup>2</sup> and its almost 100 experts are specialised in the development of inhalation products delivered by Genuair<sup>®</sup> (Almirall's dry powder inhaler) and in the design and development of new inhalation technologies. This centre has spent almost four decades dedicated to the development of inhalation products, thus making it one of the leading facilities in the field.



## **Almirall Centre of Excellence for Dermatology in Reinbek (Germany)**

This centre, which was acquired by Almirall in 2007, is located on the outskirts of Hamburg and has a total surface area of 21,000 m<sup>2</sup>. Almost 100 experts work at this facility on development programmes to find new formulations for the treatment of skin diseases. Over 60 years working in this field ranks it as a leading dermatology centre in Europe.



# **R&D** partnerships

Almirall is committed to establish alliances with public and private bodies, as well as partnerships with academic research teams and biotechnology companies all over the world, in order to spread its knowledge and innovation to the benefit of society.

In Spain Almirall has established close ties with a number of academic institutions such as the universities of Barcelona, Valencia, Santiago de Compostela and Pompeu Fabra, as well as with the Hospital Clínic of Barcelona, the Spanish National Research Council (CSIC) and the Barcelona Science Park. It also has partnerships with biotechnology companies such as Galchimia and Enantia.

On an international level, Almirall's research scientists have established a wide network of external partnerships with universities and research institutes across Europe and the United States. It has recently established alliances with the University of Michigan (USA), Imperial College London (UK), the University Hospital of South Manchester (UK) through the Medicines Evaluation Unit, and the National Institute of Health (NIH; USA). Furthermore, this network also includes partnerships with technology companies such as Mercachem (Holland), Proteros and Evotec (Germany), Charnwood and BioFocus (UK), and Aragen (USA).

### Private partnerships for establishing synergies

Almirall also promotes knowledge transfer networks with private institutions and research groups worldwide in order to create new research programmes that respond to society's current needs, and to gain access to new technology, thereby accelerating the process of identifying new drugs.

In 2012, it is worth highlighting the agreements reached with companies such as BioFocus (a subsidiary of Galapagos NV) and Aslan Pharmaceuticals. In the first case, BioFocus brought its experience in screening in a particular family of therapeutic targets to the collaboration and Almirall its knowledge of respiratory disease models, in order to jointly identify candidates for development in diseases within Almirall's therapeutic focus. Similarly, in the case of the other collaboration, Aslan Pharmaceuticals will develop Almirall's DHODH inhibitor in the Asia-Pacific region for the treatment of rheumatoid arthritis up to the completion of phase II. Once the proof of concept has been established, a global partner will be sought for phase III and subsequent commercialisation.

### Public-private partnerships for promoting innovation

Throughout 2012 Almirall made a significant effort in promoting public-private partnerships.

In Spain, Almirall has worked with Esteve and Draconis Pharma (formerly Palau Pharma) on two joint projects, Genius Pharma and Neogenius. The former was set up to develop technology platforms to facilitate the discovery of new drugs, and the latter to identify a candidate for development in the field of pain. The biotechnology company Proteomika also took part in the Neogenius project. Both projects have been partly funded by the Spanish government and have had support from public research centres such as the University of Granada, the University of Santiago de Compostela, Pompeu Fabra University, the Severo Ochoa Molecular Biology Centre, the Institute of Chemical Research of Catalonia (ICIO) and the Barcelona Science Park. Small- and medium-sized enterprises such as Enantia, Galchimia and Intelligent Pharma were also involved in the project.

At the European level, Almirall is also participating in the Innovative Medicines Initiative (IMI), a unique collaborative public-private initiative between the European Commission and European pharmaceutical companies, regulators, academia and patient organisations. Almirall is an active member of consortia working on topics closely related to its therapeutic focus. One such project is U-BIOPRED, whose aim is to identify biomarkers in order to discover more effective treatments for severe asthma.



# Global reach of Almirall's drugs

Internationalisation is one of Almirall's strategic pillars, which in 2012 accounted for almost 60 % of total sales. As a result of its growing international business activities, Almirall has consolidated the presence of its products on a global scale through its own affiliates and sales agreements with other prestigious companies in key regions, such as the United States, Japan and China.

Almirall currently has 14 affiliates and has signed agreements with trading partners in order to make its products available to prescribers and patients in countries in which they are not sold directly. Almirall's products are currently sold in over 70 countries on the five continents.

#### Spain

- The company began its business and industrial activities in 1944 in Spain, where its headquarters are located.
- Its latest launches, Tesavel®, Efficib®, Silodyx®, Solaraze® and Sativex® are making a significant contribution to revenue and are rejuvenating Almirall's product portfolio.

#### **United Kingdom-Ireland**

- Set up in January 2008, dermatological illnesses are the therapeutic focus of Almirall in the United Kingdom.
- Eklira<sup>®</sup> Genuair<sup>®</sup> was the last drug to have been added to its product portfolio in 2012.

#### Canada

 In 2012, Almirall opened an affiliate in Canada (8th biggest pharmaceutical market).

# Almirall Canada is preparing for new product launches

We will make a range of innovative drugs available to patients in Canada, particularly from our respiratory and dermatology areas.

#### Mexico

- Almirall first began operations in Latin America in 2001.
- Almogran<sup>®</sup> and Balneum Intensive<sup>®</sup> were added to the product portfolio in 2012.

#### Germany

- Operations began in 2003 and, following the acquisition of Hermal in 2007, it has become one of Almirall's largest affiliates.
- The latest products added to the catalogue were Sativex<sup>®</sup>, Actikerall<sup>®</sup> and Eklira<sup>®</sup> Genuair<sup>®</sup>, the latter of which in 2012.

#### Switzerland

- Following the acquisition of Hermal, all the rights for marketing Hermal products in Switzerland were transferred to Almirall.
- We launched Actikerall<sup>®</sup> in 2012.

### Belgium-Luxembourg

- Began operations in 1990.
- Toctino<sup>®</sup> and Sativex<sup>®</sup> were added to the product portfolio
- in 2012.

#### France

- Began operations in 2001.
- It currently sells some of Almirall's proprietary R&D drugs, such as ebastine and almotriptan, and other licensed products such as Solaraze<sup>®</sup>.

#### Portugal

Began operations in 1993.
It currently sells some of Almirall's proprietary R&D drugs, such as ebastine and almotriptan, and other licensed products.

### The Netherlands

• Began operations in 2000.

### **Nordic Countries**

- Almirall set up a new affiliate in Denmark in 2010 that sells products in five Nordic Countries (Denmark, Finland, Iceland, Norway and Sweden).
- In 2012, Eklira® Genuair® was launched in Denmark, Sativex® in Norway and Vaniqa® and Solaraze® in Iceland.

#### Poland

- The Polish affiliate was created at the beginning of 2008, following the acquisition of Hermal.
- It specialises in dermatological diseases.

### Austria

- The Austrian affiliate, which also joined the company following the acquisition of Hermal in August 2007, specialises in dermatological diseases.
- Actikerall<sup>®</sup> was added to its product portfolio in 2012.

# Italy

- Began operations in 2002.
- Specialised in dermatology, a key area for expansion, its drugs also cover the respiratory and gastroenterology areas.

# Almirall Italy celebrated its 10<sup>th</sup> anniversary

Almirall Italy has made extremely satisfactory progress during its first 10 years of operations, both in terms of the penetration of our therapeutic solutions and with regard to the growth of our organisation, which now has over 200 employees.

# **Growth platforms**

Differentiation as a competitive strategy is a reality at Almirall. Currently, Almirall's growth platforms form the basis of its specialisations, which enable us to focus on shaping our guidelines for future growth.

Our growth platforms share a common denominator: the main drugs that make them up are the result of a long process of looking into, identifying, researching and/or developing molecules in response to medical needs not yet covered; they have been innovative and differentiating, with many being first-in-class to provide real solutions for specific pathologies.

Respiratory franchise

Dermatology franchise

## **Respiratory franchise**

Eklira<sup>®</sup> Genuair<sup>®</sup> (aclidinium), a novel drug used as a bronchodilator maintenance treatment to relieve the symptoms of COPD in adult patients, is the first step towards building up a global respiratory franchise.

Almirall has set itself the target of developing a range of respiratory products that cover the main treatment options, whereby aclidinium can be used as a monotherapy or a combination therapy so that doctors are able to prescribe a wide range of treatments packaged in a single inhaler, our proprietary product, the Genuair<sup>®</sup> inhaler.

In 2012, aclidinium was approved by the health authorities in Europe and the United States. It was immediately launched in the United States, Germany, Denmark and the United Kingdom. It has been also launched in Iceland, Norway, Spain and other EU countries at the start of 2013.

In Europe, Almirall sells the product under the brand names Eklira<sup>®</sup> Genuair<sup>®</sup> and Bretaris<sup>®</sup> Genuair<sup>®</sup>, and keeps the exclusive rights in the Nordic Countries, the Netherlands, the United Kingdom and Switzerland. The Menarini Group and Quintiles hold joint rights on its commercialisation in certain territories. In the United States, Forest Laboratories sells aclidinium under the brand name Tudorza<sup>™</sup> Pressair<sup>™</sup>. In Japan the product has been under development in collaboration with Kyorin since 2012, whilst in Korea Almirall reached an agreement with Daewoong in 2012. In Australia and New Zealand it will be marketed by Invida (Menarini Group). Almirall retains the rights for the rest of the world and is still looking into securing new agreements in other key territories.

# Eklira® Genuair®

Constella<sup>®</sup>

**Eklira® Genuair®** is a step forward in the class of long-acting muscarinic antagonists (LAMA), which are the cornerstone of the treatment of COPD and are recommended for the treatment of all groups of patients. Its main benefits are:

Sativex®

- Maximum bronchodilation from the very first dose.<sup>1,2,3</sup>
- Reduced symptoms of COPD during the day, night and in the early morning.<sup>2, 4, 5</sup>
- Significant clinical improvement of breathlessness (dyspnoea).<sup>1,2</sup>
- Less use of rescue medication.<sup>1,5</sup>
- Significant clinical improvement in quality of life.<sup>1,2</sup>
- Few side effects.<sup>4, 6</sup>
- Administered in a novel multidose, dry-powder inhaler (MDPI), Genuair<sup>®</sup>.<sup>7</sup>



## **Dermatology franchise**

Almirall is currently the top pharmaceutical company to make prescription dermatology drugs in Germany and the seventh in Europe. It has held on to its leading position in recent years by launching new products such as Solaraze<sup>®</sup>, used for treating actinic keratosis caused by exposure to the sun; Balneum<sup>®</sup>, the range of products for preventing and treating dry skin and associated itchiness, and Actikerall<sup>®</sup>, prescribed for the treatment of hyperkeratotic actinic keratosis. In 2012, dermatology was one of the areas that experienced most growth. Sales accounted for 20 % of total sales with a growth rate of 8 % on the previous year.

The strategy for the future will concentrate on taking every possible opportunity to reach new agreements with other companies in order to boost the sales of our products through partnerships, add new items to our current product portfolio and/or collaborate on R&D projects focused on the treatment of inflammatory skin diseases and psoriasis.

### Main dermatology treatments

### **Actikerall**®

- Contains fluorouracil and salicylic acid.
- Prescribed for the treatment of hyperkeratotic actinic keratosis (grade I/II of severity).
- Topical solution for non-invasive lesions in the treatment of this type of non-melanoma skin cancer.

#### **Solaraze**®

- Contains diclofenac sodium and hyaluronic acid.
- Prescribed for actinic keratosis.
- Multiple action gel formulation that helps the skin's defence system to destroy damaged cells and replace them with healthy cells.

#### **Toctino**®

- Contains alitretinoin.
- Prescribed for severe chronic hand eczema that does not respond to topical corticoids.
- Oral treatment.

### Balneum<sup>®</sup> Line

 A wide range of products that mainly contain urea for full emollient treatment according to specific needs: Balneum<sup>®</sup> Intensive<sup>®</sup>, for dry and very dry skin; Plus<sup>®</sup>, for dry skin and itchiness; Kids<sup>®</sup>, for moisturising babies' skin.









"We have to put up with different types of discomfort every day and that can become very frustrating."



Angie IBS-c patient. United Kingdom

### **Constella**®

Constella<sup>®</sup> (linaclotide) was approved by the health authorities in Europe and the United States in 2012. The EMA and FDA approved the commercialisation of linaclotide as a first-in-class treatment for patients suffering from IBS-c. IBS-c is a gastrointestinal illness that is characterised by abdominal swelling and pain associated with bowel movements or altered bowel habits. In the case of IBS-c, these bowel habits are predominantly characterised by constipation.

In 2009, Almirall signed a pan-European agreement with Ironwood to sell the compound under the brand name Constella<sup>®</sup> in all European Union member states, Russia, the Commonwealth of Independent States of the former USSR (CIS), Switzerland, Norway and Turkey, as well as other countries of former Yugoslavia. Since 2012, the company has held the rights for Mexico through a license granted by Forest Laboratories. The first launches are expected to take place in the first half of 2013.

Almirall is also responsible for activities relating to final production and to obtaining regulatory approval in the abovementioned territories.

### **Constella®**

- **Constella**<sup>®</sup> is an antagonist guanylate cyclase type-C (AGCC) peptide whose dual action acts locally on the gastrointestinal tract: intestinal secretion increases and visceral pain is reduced.<sup>8, 9, 10</sup>
- This makes it possible to control the symptoms of IBS-c: abdominal pain, swelling and constipation, with a positive impact on the patient's quality of life.<sup>8, 9, 11</sup>
- It is first-in-class in the treatment of this gastrointestinal illness.<sup>10</sup>

• Clinical studies performed on 1,600 IBS-c sufferers demonstrated that it was of sustained efficacy and had a clean safety profile.



## Sativex®

Sativex<sup>®</sup> is the first new drug to appear in over 10 years for the treatment of spasticity (muscular rigidity and spasms) caused by multiple sclerosis (MS), as well as being a first-in-class drug. It is currently in development phase with three new studies to treat chronic cancer pain.

Almirall holds the commercial rights of Sativex<sup>®</sup> in Europe (except the United Kingdom) and Mexico following the agreements reached with GW Pharmaceuticals. Since then, the company has applied for regulatory approval in a number of countries through the mutual recognition procedure. Sativex<sup>®</sup> is now available as a prescription drug in Germany, Denmark, Spain and Norway. More launches have been planned for 2013.

Almirall expects to be given approval shortly so that it can begin to sell Sativex<sup>®</sup> in 10 other countries in Europe, following the recommendation to approve it in 2012 in Belgium, Finland, Iceland, Ireland, Luxembourg, the Netherlands, Poland, Portugal and Slovakia. This will contribute to strengthening its position as an innovative company that offers high value treatments with international outreach.



### **Sativex**<sup>®</sup>

- **Sativex**<sup>®</sup> is a drug with active ingredients of plant origin that is based on two cannabinoids in equal proportions: 9-delta-tetrahydrocannabinol (THC) and cannabidiol (CBD).
- This formulation delivers all of the medical benefits of cannabinoids and minimises their side effects, including addiction, intoxication, sedation and psychotropic effects. Sativex<sup>®</sup> is administered through an oromucosal spray.<sup>12</sup>
- Sativex<sup>®</sup> is a first-in-class drug and is currently the only treatment available (except for an intrathecal pump or irreversible surgery) for relieving spasticity that is resistant to oral drugs and improving the symptoms associated with treatment-resistant spasticity in multiple sclerosis (MS).
- The results obtained from daily practical clinical practices in an observational study called Mobility Improvements with Spasticity in Multiple Sclerosis 2 (MOVE 2) confirmed that patients showed clear signs of relief from spasticity and its associated symptoms, and that the drug was well tolerated.<sup>12</sup>



# **OTC** products

Almirall has a large OTC portfolio in Spain made up of products used for the treatment of minor illnesses. The Spanish government's latest removal of prescription drugs from reimbursement lists in 2012 (Spanish Royal Decree 16/2012) could be an opportunity for Almirall's OTC division, especially for its well established trademarks such as Almax<sup>®</sup>, Calmatel<sup>®</sup>, Actithiol<sup>®</sup>, Sekisan<sup>®</sup> and Rino-Ebastel<sup>®</sup>.

Almirall's OTC line of business is made up of a number of products subject to various regulatory frameworks (OTC, EXO, cosmetics, etc.). Most are mature products that have been on the market for over 20 years and, therefore, have built up leading positions in their category backed by a long track record in promotion to the healthcare community.

The OTC division is an interesting business opportunity for the company as, on the one hand, the investment in marketing is lower than for prescription drugs and, on the other hand, prices are far more flexible and can be set on the basis of the competitive edge a product has on the market. Almirall's OTC line of businesses brought in  $\in$  54 MM of sales for the company in 2012.

Given that the removal of some categories of prescription drugs from reimbursement lists at the end of 2012 affected 40 % of this line of business, our current target is to optimise and improve current margins rather than seeking to expand this line of business in the short-term.

Following the latest removal of prescription drugs from reimbursement lists such as Almax<sup>®</sup>, Calmatel<sup>®</sup>, Actithiol<sup>®</sup>, Sekisan<sup>®</sup> and Rino-Ebastel<sup>®</sup>, changes are being made to the law so that direct-to-consumer advertising campaigns can be run for some of these brands. It has therefore been planned to expand some of these lines in 2013. To summarise, Almirall's product portfolio in the EXO segment has been strengthened, which will pave the way for boosting its promotion.

Promotion focuses on the medical community (mainly primary carers, but also on paediatricians, orthopaedic surgeons and digestive specialists) and on pharmacies. Almirall is among the laboratories in Spain that pays the most medical visits to pharmacies. Over the last 15 years,

### **Almax**®

- Almax<sup>®</sup> is the leading antacid in the Spanish market and the brand is used as a generic trademark. It is one of Almirall's proprietary R&D products (active ingredient: almagate), which was launched in 1984.
- It currently comes in two presentations, the most widely sold of which are: Almax<sup>®</sup> liquid in a sachet and Almax<sup>®</sup> a chewable tablet.
- The process to regularise the summary of product characteristics began in 2012 in order to be promoted directly to the general public.

# Calmatel®

- Calmatel<sup>®</sup> is the third most popular topical NSAIA on the Spanish market. It is one of Almirall's proprietary R&D products (active ingredient: piketoprofen), which was launched in 1985.
- It is sold in three presentations: gel, cream and a solution to spray on the skin.
- The process to regularise the summary of product characteristics began in 2012 in order to be promoted directly to the general public.





the company has gradually built up its relations with pharmacies, due to they play a key role in dispensing drugs and recommending products for health self-care.

Thus, Almirall ran over 100 face-to-face training sessions in 2012 that were attended by over 3,000 pharmacists. The training courses dealt with such topics as pharmaceutical care, pharmacy management and staff management.

Almirall has a well established relationship marketing programme with pharmacies in the shape of the "Club de la Farmacia", which celebrated its ninth anniversary in 2012. The "Club de la Farmacia" enjoys an extremely good reputation amongst people who work in pharmacies. This is largely due to the ongoing efforts made by reps on their visits and the campaigns run in specialised media, both offline and online. In 2012, the Club's website (www.clubdelafarmacia.com) obtained the HONcode certification, which is awarded in recognition of the reliability of the information on health-related websites.

In 2012, Almirall helped put together the new edition of the ASPIME report, which reflects the financial performance of Spanish pharmacies.

EXO: Product excluded from Spanish Health System OTC: Over-the-counter

### **Hidroxil**®

- Hidroxil<sup>®</sup> is the leading vitamin B complex in the Spanish market. This complex, which contains vitamin B12, B6 and B1 in therapeutic doses, was launched in 1965. It is recommended as a vitamin supplement, for neuropathic pain relief and backache.
- It is sold in boxes of 30 tablets.
- It is a not financed product free price, which requires a prescription since August 2010.



- Actithiol<sup>®</sup> is the trademark that encompasses an antihistamine, a preparation for adults, another for children and a lozenge, all of which are mucolytic agents prescribed for symptoms caused by excess mucus due to coughs and nasal congestion.
- The antihistamine carries the greatest weight in the family and is the only syrup on the market that combines a mucolytic agent (carbocisteine) with an antihistamine (promethazine).
- In 2012, this was the only product in the family that had attained the status of a non-reimbursable, non-prescription drug.



### **Thiomucase®**

- Thiomucase® is the leading anti-cellulite treatment sold in pharmacies in Spain. It was originally as a prescription drug.
- In 2006, its regulatory status was changed to a cosmetic, which enabled it to be packaged in different sizes. The Thiomucase<sup>®</sup> stick for men to treat the waist and stomach was launched in 2012, thus marking the start of the trademark making inroads into the male market.
- Thiomucase<sup>®</sup> was the only anti-cellulite treatment whose sales grew last year, with a 6 % increase being recorded against the drop in sales of the market leader.



## Corporate development agreements

One of Almirall's strategic lines for growth and internationalisation is the collaboration agreements it signs with other companies in the sector in accordance with the company's strategic, geographic and therapeutic priorities.

In 2012, Almirall signed a total of eight new collaboration agreements, five of which involved the licensing of R&D proprietary products, whilst the remaining three were for collaborations in the marketing of drugs developed by other companies. A twofold approach is taken to these agreements. Firstly, they are entered into in order to boost the development and commercialisation of R&D proprietary drugs on the main markets in which these partners trade (license-out agreements). The second reason is to diversify the portfolio of drugs Almirall makes available to healthcare professionals in the countries in which it operates (license-in agreements).

## Almirall signed eight collaboration agreements in 2012 and consolidated the global presence of aclidinium

# Granting of licenses on proprietary R&D drugs

Almirall is able to strengthen its strategy of internationalisation by licensing out some of its products. In 2012, both the aclidinium monotherapy and its combination with formoterol, which are prescribed for the treatment of chronic obstructive pulmonary disease (COPD), were the main proprietary R&D products for which Almirall granted licenses. As a result, to those already granted in previous years in the United States and Japan can be added new ones in Korea, most of the European Union, Russia, Turkey, countries of the Commonwealth of Independent States (CIS), Australia and New Zealand. Almirall thus consolidated the global presence of one of its principal growth platforms.

In 2012, Almirall signed the following license agreements for its proprietary R&D products:

Compound	Pathology	Successful bidder	Countries	Agreement
Respiratory franchise (aclidinium in monotherapy and combination therapy)	Chronic obstructive pulmonary disease (COPD)	Daewoong Pharmaceuticals	Korea	Development Regulatory approval Commercialisation
Respiratory franchise (aclidinium in monotherapy and combination therapy)	Chronic obstructive pulmonary disease (COPD)	Menarini Group	European Union, (except the United Kingdom, the Netherlands and the Nordic Countries), Russia, Turkey and CIS countries	Commercialisation
Respiratory franchise (aclidinium in monotherapy and combination therapy)	Chronic obstructive pulmonary disease (COPD)	Menarini Group	Australia and New Zealand	Regulatory approval Commercialisation
Respiratory franchise (aclidinium in monotherapy and combination therapy)	Chronic obstructive pulmonary disease (COPD)	Forest Laboratories	Canada	Co-promotion
LAS186323 inhibitor	Rheumatoid arthritis	Aslan Pharmaceuticals	Global rights	Development until the end of phase II

If you wish to see the list of current agreements, go to our website at www.almirall.com

# Acquisition of licenses from other companies

By signing this type of agreement, called license-in agreements, Almirall is able to diversify its product portfolio and strengthen its commitment to society by making innovative drugs available to healthcare professionals, all of which contributes to improving people's health and quality of life. In 2012, the company signed three collaboration agreements with as many other companies, thereby strengthening, amongst others, the cardiovascular area in Spain through the co-promotion of Xarelto<sup>®</sup>, an oral anticoagulant that is recommended for preventing strokes in patients with atrial fibrillation.

The following agreements for acquiring licenses from other companies were signed by Almirall in 2012:

Trademark (compound)	Pathology	License holder	Countries	Agreement
Xarelto® (rivaroxaban)	Oral anticoagulant/ atrial fibrillation	Bayer	Spain	Co-promotion
Sativex <sup>®</sup> (CBD:THC)	Muscular rigidity in multiple sclerosis	GW Pharmaceuticals Ltd.	Mexico	Commercialisation
Constella® (linaclotide)	Irritable bowel syndrome with constipation (IBS-c)	Forest Laboratories	Mexico	Commercialisation

### **Exploring new partnerships**

In 2012, Almirall acquired an equity stake in AB-Biotics, a Spanish biotechnology company specialised in genetics. The operation enabled AB-Biotics to fund a number of studies in this field and promote its internationalisation. Almirall was in turn able to expand its portfolio of innovative projects and has promised to take part in the promotion and marketing in Spain of Neurofarmagen<sup>®</sup>.

Using a sample of saliva, this genetic test makes it possible to identify the predisposition of a subject to the most common compounds prescribed for the treatment of depression, schizophrenia, bipolar disorder and epilepsy.



## **Business year sales**

In 2012, Total Revenues (€ 900.2 MM) for the year rose by 3 % on 2011, Net Sales totalled € 682.9 MM (11.1 % down on 2011), whilst our international sales now account for 60 % of total sales and are growing at a rate of 5 % per annum.

Specifically, Total Revenues rose to  $\leq$  900.2 MM, a 3.1 % increase driven by Other Revenues of  $\leq$  217.3 MM. This was mainly due to the milestone associated with the approval of the aclidinium monotherapy in the United States and Europe being entered into the books.

The Other Revenues item covers one of the lines of our business model as it includes the amounts received through agreements with partners and is linked to both our pipeline and the royalties earned from our proprietary products, as well as to co-promotions of products licensed out from third parties. Net Sales totalled  $\in$  682.9 MM due to the cuts in public health spending in Spain and competition from generic drugs. International sales grew by 5 % on 2011 and account for almost 60 % of total sales. It is worth highlighting that 85 % of these sales are made directly through affiliates.

Following the opening of our new affiliate in Canada, we now have 14 affiliates, which means we have sales networks in 22 countries spread across Europe and North America. Almirall's process of internationalisation is still one of its strategic priorities and it is anticipated that its growing international trade will account for over 70 % of its business by 2014.

# Total Revenues € 900.2 MM

Net Sales € 682.9 MM ~ **60 %** of International Sales

### Net sales by distribution model

In 2012, 41.5 % of sales ( $\notin$  283.1 MM) were made in Spain and 43 % ( $\notin$  293.9 MM) through international affiliates. Therefore, almost 85 % of the sales in the year were achieved through Almirall's affiliates.

### Net sales by distribution model

Rounded to nearest million euros	2012
Almirall's direct sales (Spain)	283.1
Almirall's direct sales (other affiliates)	293.9
Licensee sales	87.8
Corporate sales <sup>(1)</sup>	18.0
Total	682.9



(1) Toll manufacturing and other sales.

### Net sales by geographical area

A breakdown of sales by geographical area shows that they have dropped slightly in Europe (-2.4 %), particularly in Spain (-27.0 %), although they have increased significantly (33.8 %) on the previous year in America, Asia and Africa.

### Net sales by geographical area

Rounded to nearest million euros	2012
Spain	283.1
Europe*	284.2
Africa, America and Asia	97.6
Corporate sales	18.0
Total	682.9
*Includes the Middle East	



\*Includes the Middle East.

Pounded to pagrast milli

### Net sales by therapeutic area

Almirall is a leader in sales in its key therapeutic areas (respiratory, dermatology and gastrointestinal) and they account for 65 % of total sales.

### Net sales by therapeutic area

Rounded to nearest million euros	2012
Respiratory	173.4
Gastrointestinal	147.2
Dermatology	130.2
Central nervous system	83.2
Cardiovascular	63.9
Musculoskeletal	45.8
Urology	18.7
Other therapeutic areas	20.5
Total	682.9



### A well-balanced product portfolio

Almirall's 15 top-selling brands accounted for almost 70 % of net sales and no single product exceeds 15 %, which reflects a balanced portfolio without over-exposure to a single product.

Almirall's product portfolio is highly diverse in terms of geographical and therapeutic areas, and well-balanced in terms of proprietary R&D and licensed products.

Of the 15 top-selling products in 2012, nine were proprietary products: Airtal<sup>®</sup>, Almax<sup>®</sup>, Almogran<sup>®</sup>, Balneum<sup>®</sup>, Cidine<sup>®</sup>, Cleboril<sup>®</sup>, Decoderm<sup>®</sup>, Ebastel<sup>®</sup> and Eklira<sup>®</sup> Genuair<sup>®</sup>.

ou	nded to nearest million euros		2012
٢	Ebastel® and others (ebastine)	90.9	13.3 %
٢	Almogran <sup>®</sup> and others (almotriptan)	52.3	7.7 %
	Plusvent® (salmeterol + fluticasone)	49.3	7.2 %
	Tesavel® & Efficib® (sitagliptin/ sitagliptin + metformin)	43.9	6.4 %
	Solaraze® & Actikerall® (diclofenac/5-fluorouracil + salicylic acid)	33.0	4.8 %
	Parapres® (candesartan cilexetile)	32.0	4.7 %
٢	Airtal® and others (aceclofenac)	28.9	4.2 %
٢	Eklira® Genuair® and others (aclidinium)	27.0	3.9 %
٢	Decoderm <sup>®</sup> and others (fluprednidene)	19.6	2.9 %
٢	Balneum <sup>®</sup> and others (urea)	18.2	2.7 %
٢	Almax® (almagate)	17.2	2.5 %
	Pantopan® (pantoprazole)	15.8	2.3 %
٢	Cidine <sup>®</sup> and others (cinitapride)	15.3	2.2 %
٢	Cleboril® (clebopride)	13.8	2.0 %
	Elecor® (eplerenone)	13.1	1.9 %
	Other	212.5	31.1 %
	Total	682.9	100 %

Almirall has a diverse catalogue of branded products

## **Production**

Almirall's industrial organisation ensures that quality products are manufactured in the amounts and within the timeframes required to meet the global demand for our products at an optimum cost.

### **Consolidation of production plants**

The industrial area faced enormous challenges in 2012. Following the streamlining of our pharmaceutical plants, a process that was concluded in Spain in 2011, we have managed to consolidate and streamline our production plants so that they are able to respond to the market's changing demands in an increasingly uncertain environment, whilst delivering high levels of cost-effective service and guality. Against this backdrop, we have kept up our projects to transfer products from one plant to another so that they are able to hone their specialisations, thereby giving the group a competitive edge. In addition to this, we have added a sound risk management system to monitor production. This enables us to successfully rise to the challenge of manufacturing new products and concentrating on those that bring in the biggest turnover for the company.

### **Ready for new launches**

Our involvement in the launch of aclidinium and linaclotide in a number of regions was an exciting challenge.

The beginning of the year was a particularly intense time as the FDA was to inspect the chemical plants where we manufacture the compound aclidinium, a mandatory requirement for its approval in the USA. The inspection was successfully passed. The active ingredient was manufactured throughout the year and regular supplies sent to the USA in order to ensure its launch at the end of the year would go smoothly. Following a concerted effort to obtain regulatory approval in Europe in July, all of the work required to be able to launch the product was done in record time so that it could be made available as quickly as possible for the first time in Europe: Denmark in September, and United Kingdom and Germany in October 2012.

In anticipation of the regulatory approval of linaclotide in Europe, which was finally obtained in November, all of the certificates and other procedures necessary to ensure its successful launch in 2013 were also processed.



Pharmaceutical plant in Sant Andreu de la Barca (Barcelona, Spain)



# SOCIAL COMMITMENT

Promoting the knowledge of healthcare professionals to the benefit of their patients, providing a better working environment for all employees and collaborators and reducing the environmental impact of its business operations are Almirall's main commitments to society.

• 56 Our commitment to society • 60 Our team, Almirall's best asset

• 62 Committed to health and safety and the environment

# Our commitment to society

At Almirall, we believe that part of our responsibility lies in putting our knowledge across to society about the therapeutic areas in which we specialise. To fulfil this commitment, we promote training and scientific dissemination activities for professionals and do everything we can to encourage the general public to adopt healthy habits. We are also actively involved in a number of social projects.

# Training and scientific dissemination activities

At Almirall, we consider that working in collaboration with healthcare professionals is essential to advancing their knowledge of the illnesses we treat.

We believe that promoting meetings with healthcare workers so that we can exchange opinions with them, find out first-hand what their professional needs are and explain the benefits of our drugs to them are an extremely useful tool for giving them the best possible service we can offer.

- In addition, the "Club de la Farmacia" website (www.clubdelafarmacia.com), which now has over 73,906 registered users, had over 123,500 hits, an 88.3 % increase in users and a 47.7 % increase in hits in comparison with 2011.
- We should highlight our commitment to young professionals, who are able to build up their experience thanks to our platforms at <u>www.trainmed.com</u> and <u>www.comunidadresidentes.com</u>, which provide doctors in training with tools for improving their professional development.

published

**14** scientific papers

**115** training courses



In 2012, we taught 115 training courses in Spain that were attended by 3,800 students, 58 workshops were run to which over 1,300 people came and we scheduled over 90 medical meetings that proved to be extremely popular with the medical community, as reflected by the attendance figures of over 4,900 people.

We round off the face-to-face training given to healthcare professionals through a number of online platforms, which have been developed both internally and through the sponsorship of projects run by third parties.

• The portal for healthcare professionals hosted by Almirall in Spain (<u>www.solucionesalmirall.com</u>) has over 38,743 registered users who in 2012 visited the site over 62,703 times, an increase of 2.2 % in comparison with 2011.



In the field of science, our employees have published 14 papers in the leading journals of their areas of specialisation, such as the European Respiratory Journal, and they have given talks at conferences, as was the case of that delivered at the Respiratory Drug Delivery, the world's leading specialised conference on inhalers.

Moreover, we have published 21 posters and have worked on 12 projects organised by different scientific societies and professional associations, amongst which it is worth highlighting our participation in the annual congress of the German Society of Pneumology and our collaboration with the Spanish Society of Respiratory Diseases (SEPAR) in organising the 8th symposium on these types of pathologies in Barcelona.

Our commitment to clinical research also includes the financing of projects related to one of our areas of specialisation: multiple sclerosis. In 2012, we awarded two grants of 24,000 euros each for the second year running to two projects that focused on muscular rigidity, or spasticity, one of the symptoms of this neurological disorder.

- The first is supervised by doctor Thorsten Schultheiß from the Department of Neurology at the University Hospital of Dresden (Germany). It will assess the efficacy of Sativex<sup>®</sup> based on three criteria: gait parameters, the effect on patients' fatigue and level of depression.
- The second, supervised by M<sup>a</sup> del Carmen Molina from the Rehabilitation Department at the University Hospital of Nuestra Señora de la Candelaria, in Santa Cruz de Tenerife (Spain), will assess how much the quality of life of patients who do their rehabilitation exercises via videoconference improves in comparison with those who do them without the help of this supervision. In both cases, it is anticipated that the results will be published in the second quarter of 2013.

Our reps likewise make medical calls to give healthcare professionals first-hand, ethical and transparent information about our products.

At Almirall, we operate in strict compliance with the ethical codes for promoting medicines that are drawn up by the pharmaceutical industry's professional associations in all of the countries in which we operate.

## Promoting meetings with healthcare professionals is essential to understanding their needs



However, our ties with the medical and research community are not purely limited to giving out information. We also take a concern in the quality of life of its members.

Almirall has signed collaboration agreements with the Patronato de Huérfanos y Protección Social de Médicos Príncipe de Asturias Foundation, and the Galatea Foundation. The aim of these agreements is to raise awareness amongst junior doctors, their tutors and supervisors of the importance of looking after their health. We are very actively involved in the organisation of round table sessions at which the psychosocial risks of practising this profession are examined and the skills that should be developed or strengthened in order to deal with these risks are discussed.

Thus, in 2012 we conducted a study of over 200 junior doctors in hospitals across Catalonia, in which their lifestyles and eating habits were examined, as were their mental health and working environment. From the conclusions reached, it is worth highlighting the need to encourage the members of this group to adopt healthier lifestyle habits, as this would both have benefits on their health and would serve as a way of setting an example to the patients they treat at their worksites.



# Encouraging patients to adopt healthy habits

Our social commitment is not limited to the medical community. Patients and their environment are also the focus of our outreach activities.

At Almirall, we are convinced that encouraging people to adopt healthy lifestyle habits is essential to improving the quality of life of the population as a whole and to reducing the economic impact of pathologies such as chronic obstructive pulmonary disease (COPD) on the sustainability of the national health systems in the countries in which we operate.

The Internet has become a fundamental communications channel for promoting healthier lifestyles. In 2012, we managed to consolidate a number of online platforms on which we provide useful, updated information to patients and their families about the various pathologies Almirall treats.

- The website <u>www.cuidatusalud.com</u>, which was created to provide comprehensive information about the illnesses for which Almirall delivers solutions, had 107,332 hits in 2012, up by 54.2 % on the previous year.
- The website specialising in multiple sclerosis <u>www.vivirconem.com</u> and its English version <u>www.lifeandms.com</u> respectively received 43,941 and 6,232 visits, which translate as an 8.2 % and 289.2 % increase respectively, in comparison with 2011.
- The website <u>www.nohaydolor.com</u>, which was set up to provide information about the prevention, identification and treatment of any type of minor injury that may be sustained by people who play sports, had 152,836 hits in 2012, a 64.5 % increase on the previous year.
- The Thiomucase website (<u>www.thiomucase.es</u>) provides practical tips about cellulite and information about this product developed by Almirall. In 2012, we managed to exceed the figure of 146,899 registered users and 201,755 hits, a 29.9 % and 29.6 % increase, respectively, in comparison with 2011.

We promote healthy lifestyles to improve the quality of life of patients Our commitment also extends to patients through a number of initiatives, such as taking part in World Diabetes Day and World COPD Day, for which we run activities to prevent and raise awareness about these diseases.

Our concern for patients was recognised in 2012 with the award of an international prize. The campaign conducted to ensure the proper delivery of Sativex<sup>®</sup> courses of treatment, prescribed for reducing the muscular rigidity (spasticity) caused by multiple sclerosis, received an accolade in the shape of a Galien award at the 21st edition of the awards in Spain, in the category «Best Patient Care 2011». These awards for medical research first originated in France in 1970. Since then, 12 other countries have taken up the initiative of awarding these highly prestigious prizes, which have gained worldwide recognition.



## International recognition for our concern about our patients

### **Collaborations with other not-for-profit organisations**

Almirall's social commitment also means become more involved in the socio-economic and cultural realities of the underprivileged countries. Since 2008, we have been actively involved with the Vicente Ferrer Foundation, both by training staff in healthcare centres and by providing funding to it. Thus, in 2012 we collaborated in the building work on 10 homes in Anantapur, the region in India in which this institution is based.

Furthermore, since 2004 we have sat on the board of trustees of the Integra Foundation, which is devoted to promoting work placements for people in a position of social exclusion.



## Our team, Almirall's best asset

In 2012, Almirall had over 2,800 staff of 20 different nationalities. Given the cultural and geographic diversity of our company, promoting the professional and personal development of our employees in a cohesive manner by involving them in a common project is Almirall's top priority.

The CRF Institute, an international independent organisation dedicated to assessing human resources policies in businesses ranked Almirall as a "Top Employer" for the fifth time running in 2012. This recognition underscores our commitment to working with innovative management models that have resulted in better working conditions for our employees.

The main factor that underpins the success of a business is its team. Based on this premise, at Almirall we consider the continuing training of our employees as a pillar that sustains the long-term growth of the company. Promoting their professional and personal growth in different disciplines, in an open working environment that offers equal opportunities to all employees regardless of their status, forms the bedrock of our commitment to them.

In 2012, we ran 100,000 hours of training courses devoted to the development of our employees. Of the total number of hours devoted to training, the following can be highlighted:



### **Talent at Almirall**



**70 %** of employees expert in the pharmaceutical sector

**20**-plus different nationalities

20% of employees devoted to R&D

62 % of employees with university qualifications

**50% 50%** Women

**14** years of experience at Almirall Spain on average

This is a commitment that we consider to be a mutually beneficial arrangement. Our 2012 figures show that the average length of service of Almirall's staff was 14 years in Spain and 7 years on an international level, which denotes the organisation's great ability to retain its talent. In fact, last year Almirall recognised the work of 237 employees who had followed their career path at the company for between 10 and 25 years. There is also a practically even distribution of staff in terms of gender. Thus, 49.6 % of Almirall's employees are men and 50.4 % are women. Of the total number of employees, 70 % are experts in the pharmaceutical sector and over 60 % have had a university education.



Almirall: top employer

Talent retention is set off by the new professionals who join the organisation, whose skills enrich the way it operates. To this end, Almirall has signed collaboration agreements with leading universities and business schools in order to give young people in education new opportunities to join the job market.

# Committed to health and safety and the environment

Our task in this area is to safeguard the health and safety of our employees and to respect the environment. Indeed, we encourage our employees to realise these ideals on a daily basis and our business is subject to continual assessments in order to attain maximum levels of efficiency.

In 2012, we completely merged our corporate occupational hazard prevention programme with the management of our environmental and energy affairs into a single common policy.

Almirall is therefore now governed by the following basic principles:

- Its commitment to the prevention of occupational hazards and contamination by encouraging employees to make these ideals a part of their daily routines.
- Its commitment to the ongoing improvement of our environmental and health and safety management, in line with the legal requirements in force and other requirements to which Almirall adheres voluntarily.
- Its efficient and rational management of natural resources, such as raw materials, energy and water, through the promotion of energy and water savings, and efficient processes.
- The introduction of regular environmental and health and safety management programmes with goals and targets in line with current legislation, the company's occupational hazard prevention and environmental policy, and the potential improved uses of energy identified.
- The training, involvement and participation of employees and companies that work with Almirall in the application of the principles contained in this policy.
- The availability of the information and resources necessary, and the drawing up of plans to ensure they are properly implemented.
- Occupational hazard prevention and respect for the environment is a goal shared by the whole of the company and, therefore, all of the people who work for it are responsible for achieving it whatever their seniority or post.

## Occupational hazard prevention

Our occupational hazard prevention policy, which is assigned all of the resources necessary to ensure it is effectively implemented, reflects our commitment to the team that makes up Almirall. One of our principles is to promote the assimilation of occupational hazard prevention practices by our employees in their jobs on a daily basis.

In 2012, training courses were run that accounted for a total of 3,800 teaching hours. In addition, we are convinced that promoting healthier lifestyles is also a way of improving health and safety at the workplace. Thus, a number of prevention campaigns have been conducted on our worksites through our medical service. We also ran an international awareness-raising campaign on road safety, which received the 2012 International Fleet Safety Award.

At Almirall, we regularly conduct assessments on the occupational risks of all work stations and worksites, check specific health and safety issues to ascertain compliance with industrial hygiene and ergonomics, as well as review the performance of internal and external audits. Specifically, 270 occupational risk assessments were conducted on work stations and worksites, and 140 inspections and internal audits carried out in 2012.

As a result of these efforts, since 2007 Almirall has held the TÜVRheinland certificate, which attests to the compliance of our occupational hazard prevention management system with the international health and safety standard, OHSAS 18001:2007.

In 2012, we successfully completed our second annual follow-up audit and our production plants and R&D centres in Germany have implemented the corporate management system in accordance with the abovementioned quality standard.



At Almirall we apply the strictest international standards

# Sustainable management of the environment

The implementation of energy efficiency solutions at our production plants, R&D centres and offices, and the rational management of natural resources and the recycling of waste generated are at the heart of our environmental strategy. All measures taken are compliant with the international standard ISO 14001:2004, the quality certificate that recognises the application of the very highest standards of management, which go well beyond the criteria used to deal with such matters under Spanish law.

Almirall Spain has been awarded the international TÜVRheinland certificate since 2004 for its R&D activities, the manufacture of its active ingredients and the manufacture of its pharmaceutical products. In 2012, we successfully completed our second annual follow-up audit and our production plants and R&D centres in Germany have implemented the corporate management system in accordance with the abovementioned quality standard.

In 2012, we also implemented an energy management system in all of our worksites in Spain in compliance with the new international standard ISO 50001:2011, which is due for an audit in the first half of 2013. The implementation of this system will enable us to make a more efficient use of energy, with the subsequent reduction in the environmental impact of our business activities.

Our environmental policy is based on four key criteria for reducing the impact of our worksites on the environment: prevention, recycling, monitoring and the involvement of employees and the companies that work with us.

In order to meet our commitment, at Almirall we have implemented eco-efficient solutions in our production plants throughout the process: from the pre-selection of the materials that we use to make our products to the use of more environmentally friendly sources of energy at our worksites, through to the subsequent recycling and reuse of the waste generated. Our environmental control systems therefore monitor the whole of the production process.

As a result of our efforts, last year we reduced the amount of greenhouse gas emissions from the power used at our production plants and R&D centres in Spain by 3 %, with the 7 % reduction at the R&D centre in Sant Feliu being worthy of special mention.

Likewise, thanks to Almirall's commitment to optimising its manufacturing processes by minimising the use of

solvents, since 2008 we have reduced the consumption of these substances in our production plants and the associated emissions by 30 %.

With regard to volume of waste, we have managed to reduce the amount of non-recoverable and non-hazardous waste by 30 % over the past four years. This is a clear indication of the improvements made in minimising and sorting general waste at our worksites, thus resulting in more waste being recycled.

In the case of confidential documentation and the recovery of toners, since 2008 Almirall has had a collaboration agreement in place with Femarec, a not-for-profit organisation devoted to the social, labour and cultural integration of groups at risk of social exclusion that specialises in the recycling of this type of material.

Furthermore, as a company in the pharmaceutical sector, our commitment to the environment includes partnerships with a number of local and/or national organisations in the countries in which we operate whereby medicines used in the home are either recycled or subject to waste management. For example, in Spain we are a member of SIGRE, a not-for-profit organisation set up for this purpose, whilst in France we have signed up to the CYCLAMED collection programme.





# FINANCE AND STOCK PERFORMANCE

We hit our targets in a complex environment. Almirall's sound, privileged financial position will enable it to take on new challenges and expansion projects.

• 66 Financial highlights in 2012 • 68 Functional Income Statement

• 70 Balance Sheet • 71 Cash Flow • 72 Almirall on the Stock Exchange

# Financial highlights in 2012

The results for 2012 were in line with forecasts and reflect the impact of the cutbacks in health spending in Spain, the growing competition from generic drugs, the investments made in R&D and new product launches.



1 Earnings per Share. 2 Rounded figure. Shareholders will be able to choose between a cash payout or scrip dividend shares. 2012 was a landmark year for Almirall that marked a turning point in establishing the conditions for sustained growth in the mid to long-term As expected, sales dropped by 11.1 % falling to  $\in$  682.9 MM, which was mainly due to the performance of the Spanish market. Despite this and thanks to Other Income, which amounted to  $\in$  217.3 MM, the company's Total Revenues rose by 3.1 % to  $\in$  900.2 MM.

Following the opening of our new affiliate in Canada, we now have 14 affiliates, by which we have direct sales capabilities in 22 countries spread across Europe and North America. Almirall's international operations are continuing to grow and now account for almost 60 % of our total business, in comparison with 50 % the previous year. Almirall's process of internationalisation is still one of its strategic priorities and it is anticipated that international trade will account for over 70 % of its business by 2014.

We have also strengthened our business with trading partners, particularly for aclidinium. We have granted the trading rights for this drug to the Menarini Group in several European countries, as well as in Australia and New Zealand, whilst the rights have been granted to Daewoong in Korea and to Forest in Canada and the USA. As a result of these agreements, our direct and indirect trade in aclidinium covers for 90 % of the global market. Some of these agreements have brought an income as a result of milestone reached, as reflected under the heading Other Income.

The decline in sales and the increased spending on R&D and SG&A have entailed a decrease in EBIT and EBITDA (-42.2 % and -22.5 %, respectively), which totalled  $\in$  56.0 MM and  $\in$  124.0 MM, respectively, in a context of significantly higher marketing budgets for the launch of new products.

Normalised Net Income reached  $\in$  77.8 MM (-20.5%), in line with forecasts, whilst Net Income reached  $\in$  76.4 MM (-9.3 %).

The Cash Flow from operations totalled  $\in$  112.8 MM. Almirall has continued to strengthen its solid Balance Sheet with its equity, which now accounts for 68 % of its total assets. As regards the Financial Debt, as at 31 December 2012 it had been totally amortised. At the 2012 closing, Almirall's Cash position stood at 52 MM.

To summarise, in 2012 the group worked to adapt to the new environment so that it could continue to pursue its strategic priorities: enhancing R&D, growing internationally and maintaining its leading position in Spain.



# **Functional Income Statement**

	2012	2011	% Var
Total Revenues	900.2	873.1	3.1 %
Net Sales	682.9	768.4	(11.1 %)
Other Income	217.3	104.7	107.5 %
Cost of Goods	(262.2)	(291.1)	(9.9 %)
Gross Profit	420.7	477.3	(11.9 %)
% of sales	61.6 %	62.1 %	
R&D	(159.5)	(144.5)	10.4 %
% of sales	(23.4 %)	(18.8 %)	
SG&A	(420.5)	(340.4)	23.5 %
% of sales	(61.6 %)	(44.3 %)	
Other Operating Expenses	(2.0)	(0.2)	n.m.
% of sales	(0.3 %)	(0.0 %)	
EBIT	56.0	96.9	(42.2 %)
% of sales	8.2 %	12.6 %	
Depreciation and Amortisation	68.0	63.2	7.6 %
% of sales	10.0 %	8.2 %	
EBITDA	124.0	160.1	(22.5 %)
% of sales	18.2 %	20.8 %	
Sale of Non-Current Assets/Other	(0.5)	(2.7)	(81.5 %)
Restructuring Costs	0.0	(9.9)	(100.0 %)
Impairment Reversal/(Losses)	(2.0)	(7.0)	(71.4 %)
Net Financial Income/(Expenses)	(4.6)	(5.3)	(13.2 %)
Profit Before Tax	48.9	72.0	(32.1 %)
Corporate Income Tax	27.5	12.2	125.4 %
Net Income	76.4	84.2	(9.3 %)
Normalised Net Income	77.8	97.9	(20.5 %)
Earnings per Share (€) (1)	€ 0.45	€ 0.51	
Normalised Earnings per Share (€) (1)	€ 0.46	€ 0.59	

(1) Number of shares at the end of the period. n.m.: not material.

# Comments on the Functional Income Statement

In 2012, Almirall's Total Revenues reached  $\in$  900.2 MM, which translates as a 3.1 % increase on the previous business year. This figure includes Net Sales and Other Income. Net Sales dropped by 11.1 % to  $\in$  682.9 MM. This decline had been anticipated and is mainly due to the downturn of the Spanish market (-27.0 %) resulting from the measures to cut back on public spending on health in Spain and the growing competition from generic drugs.

By regions, the group's sales dropped slightly both in Europe and in the Middle East (-2.4 %), whilst in America, Asia and Africa they increased significantly (33.8 %). On a global level, ebastine stands out as Almirall's top selling product ( $\leq$  90.9 MM), whilst Solaraze<sup>®</sup> and Tesavel<sup>®</sup>/Efficib<sup>®</sup> are the products that showed most growth over the year (22.7 and 19.2 %, respectively). In contrast, the decline in sales of Parapres<sup>®</sup> (-33.2 %) was due to competition from generic drugs as of mid-2012.

Other Income ( $\notin 217$  MM), which includes revenue from co-development and co-promotion arrangements, increased by 107.5 %, mainly due to the income received of milestones reached for aclidinium's authorisation in the USA and Europe.

R&D expenditure increased to  $\in$  159.5 MM due to the costs associated with the development of the aclidinium + formoterol combination, whose phase III is expected to end in the second quarter of 2013. The company expects that R&D expenditure will be considerably lower over the next two years than they were in 2012.

SG&A amounted to  $\in$  420.5 MM, which is a substantial increase (23.5 %) on the previous year. This reflects the growing cost of marketing the launch of new products, specifically of aclidinium and linaclotide.

As a result of the incremental expenses in R&D and SG&A, EBIT and EBITDA decreased by 42.2 % and 22.5 %, to reach € 56.0 MM and € 124 MM, respectively.

In contrast to the previous business year, no restructuring costs were booked, but a  $\in$  2 MM loss was reported due to impairment of certain assets acquired from Shire related to the dermatology area, given their lower sales potential.

The financial profits improved in comparison with 2011, which reflects the gradual easing of debt owing to the bank in 2012, which had been totally amortised at 31 December.

Corporate Income Tax in 2012 was subject to a rebate as a result of the lower profits before tax, combined with the deductions to which the company is entitled for its R&D activities.

As a result of this, the total Net Income was  $\in$  76.4 MM, with a 9.3 % drop in comparison with the previous year, whilst the Normalised Net Income decreased by 20.5 %, thus totalling  $\in$  77.8 MM (adjusted for non ordinary items), in line with what had been anticipated.

Almirall's total revenue in 2012 was € 900.2 MM (+3.1%)

# **Balance Sheet**

2012 BALANCE SHEET	Rounded to nearest million euros		
	2012	% of BS	2011
Goodwill	270.3	19.9 %	271.1
Intangible Assets	358.2	26.4 %	353.1
Property, Plant and Equipment	157.0	11.6 %	152.1
Financial Assets	8.8	0.6 %	8.5
Other Non-Current Assets	251.4	18.5 %	213.1
Total Non-Current Assets	1,045.7	77.1 %	997.9
Inventories	92.4	6.8 %	93.2
Accounts Receivable	98.8	7.3 %	106.0
Cash and Equivalents	52.3	3.9 %	228.9
Other Current Assets	66.9	4.9 %	30.6
Total Current Assets	310.4	22.9 %	458.7
Total Assets	1,356.1		1,456.6
Shareholders' Equity	923.7	68.1 %	854.7
Financial Debt	0.0	0.0 %	202.2
Non-Current Liabilities	183.0	13.5 %	188.3
Current Liabilities	249.4	18.4 %	211.4
Total Equity and Liabilities	1,356.1		1,456.6

## **Comments on the Balance Sheet**

Following the total amortisation of the Financial Debt at the end of 2012 and the healthy Cash Flow, the company still enjoys a strong financial position. The dividend proposal to the AGM 2013 of  $\in$  0.15 gross per share (rounded figure) included an option whereby shareholders would be able to choose whether to collect their dividends in cash or as scrip dividend shares.

The following paragraphs highlight the most noteworthy aspects of the group's Balance Sheet as at 31 December 2012.

The heading Intangible Assets includes the milestones made on Sativex<sup>®</sup> in 2012 and the capitalisation of a certain research project for a respiratory product.

The position of Other Non-Current Assets of € 251.4 MM includes the tax credits that are mainly attributable to the accumulated deductions of R&D, whose effective benefits will be noticed in subsequent years.

The Inventory item remains stable despite the increased stock for new product launches.

In Liabilities, there is an increase in Shareholders' Equity (accounting for 68 % of the Balance Sheet) due to the effect of:

- Net Income for the period of  $\in$  76.4 MM.
- A dividend payout of  $\in$  1.2 MM.

## **Cash Flow**

2012 CASH FLOW	Rounded to nearest million euros		
	2012	2011	
Profit before Tax	48.8	72.0	
Depreciation and Amortisation	68.0	63.2	
Change in Working Capital	35.1	(6.6)	
Other Adjustments	(39.1)	(28.5)	
Cash Flow from Operating Activities (I)	112.8	100.1	
Financial Income	3.5	8.5	
Investments	(80.8)	(38.5)	
Divestments	0.9	2.7	
Cash Flow from Investing Activities (II)	(76.4)	(27.3)	
Finance Expense	(7.9)	(14.7)	
Dividend Distribution	(1.2)	(47.4)	
Debt Increase/(Decrease)	(202.2)	(90.4)	
Other Cash Flows	(1.6)	(4.3)	
Cash Flow from Financing Activities	(212.9)	(156.8)	
Cash Flow generated during the period	(176.5)	(84.0)	
Free Cash Flow (III) = (I) + (II)	36.4	72.8	

## Comments on the 2012 Cash Flow

Cash Flow from Operating Activities showed an increase of 13 % on the previous year, despite the lower profits before tax. The improved performance is due to the effective management of the Working Capital.

Free Cash Flow reached € 36.4 MM in 2012.

# Contents of the External Auditors' Report

The external auditors' report issued by PriceWaterhouse Coopers on 22 February 2013 contains an unqualified positive opinion with no reservations on the Consolidated Financial Statements for 2012, which include the following documents:

- Consolidated Balance Sheet as at 31 December 2012.
- Consolidated Income Statement.
- Consolidated Statement of Comprehensive Income.
- Consolidated Statement of Changes in Equity.
- Consolidated Cash Flow Statement.
- Notes to the Consolidated Financial Statement.

The full contents of the 2012 Consolidated Financial Statements, the notes to the accounts and the auditors' report can be found at <u>www.cnmv.es</u> and at <u>www.almirall.com</u>

## Almirall on the Stock Exchange

At the 2012 closing, the Almirall share price was quoted at € 7.45, which translates as a revaluation of over 40 %. The approval of aclidinium in the United States and of linaclotide in Europe by the European authorities was one of the factors that led to the excellent share price performance, which outperformed the IBEX 35.

In 2012, European governments stepped up the fiscal consolidation process intended to avert the sovereign debt crisis that is being experienced across the whole of the continent. This process has resulted in slower economic growth in the eurozone, which has either seen the return of recessions or a downturn in the economy of individual countries.

This situation was faithfully reflected on the stock markets. Thus, whilst Germany's DAX Xetra and France's CAC-40 underwent a revaluation of over 29 % and almost 15 % in 2012, respectively, the indices of the economies in the eurozone most exposed to the sovereign debt crisis could be found at the opposite extreme.

Almirall, however, outperformed the IBEX 35. The company's shares closed the year with a revaluation of over 40 %. The good news announced by the company for the respiratory and gastrointestinal areas, plus the gradual internationalisation of the business, have mitigated the effects of the policies to cut back on public spending on drugs in Spain.

Thus, the approval of aclidinium, a compound prescribed for the treatment of chronic obstructive pulmonary disease (COPD), in Europe and the United States, and the authorisation of the European Medicines Agency (EMA) to market linaclotide, a drug prescribed for the treatment of irritable bowel syndrome with constipation (IBS-c), were some of the deciding factors in the excellent performance of the share price in 2012.



Source: Thomson Reuters / Infobolsa

## Capitalisation volume and prices

Almirall closed 2012 with a share price of  $\in$  7.45, which translates as a revaluation of over 40 % in the year.

As a result, Almirall's market capitalisation in 2012 totalled  $\notin$  1,270,394 MM.

The highest price at the close of trading for Almirall shares in 2012 was  $\in$  7.65, which was recorded on 27 December, whilst the lowest price recorded was  $\in$  5.05 on 5 January.

As regards trading volumes, the total volume in 2012 reached  $\in$  211,995 MM, which translates as a 23 % drop on the previous year.

Year closing (euros)	7.45
Highest intraday level (euros)	7.79
Lowest intraday level (euros)	4.79
Annual volume (number of shares)	34,448,390
Average daily volume (number of shares)	131,986
Annual volume (euros)	211,995,231
Daily average volume (euros)	812,242
Trading days	261
Number of shares	170,522,827

### Almirall share price in 2012: main indicators

The share price underwent a revaluation of over 40 % in 2012, in comparison with the decline of over 5 % recorded by the IBEX 35 in the period

Source: Thomson Reuters / Infobolsa

Month	Trading days	Closing price	Monthly variation (in %)	Highest	Date	Lowest	Date	Daily average volume (shares)
January	22	5.22	-1.60 %	5.30	02/01/2012	5.05	05/01/2012	98,039
February	21	6.24	19.37 %	6.44	24/02/2012	5.29	01/02/2012	262,067
March	22	6.35	1.87 %	6.47	13/03/2012	6.10	22/03/2012	203,553
April	21	6.30	-0.77 %	6.45	02/04/2012	6.07	19/04/2012	187,768
Мау	23	5.64	-10.55 %	6.39	02/05/2012	5.60	24/05/2012	111,051
June	21	5.66	0.35 %	5.68	07/06/2012	5.35	26/06/2012	142,097
July	22	6.30	11.31 %	6.50	30/07/2012	5.66	23/07/2012	168,365
August	23	6.03	-4.29 %	6.36	01/08/2012	5.90	24/08/2012	71,903
September	20	6.06	0.50 %	6.58	14/09/2012	5.90	26/09/2012	99,743
October	23	6.90	13.86 %	6.97	30/10/2012	6.15	01/10/2012	59,570
November	22	7.12	3.19 %	7.12	30/11/2012	6.53	08/11/2012	53,284
December	21	7.45	4.63 %	7.65	27/12/2012	7.16	06/12/2012	139,695

## Performance of Almirall share price on the stock exchange

Source: Thomson Reuters / Infobolsa



## Share capital and dividends

Almirall began trading on the Spanish Stock Exchange on 20 June 2007. On 4 May 2012, the company's AGM approved a payout of a scrip dividend of  $\in$  0.18 gross per share (rounded figure), redeemable in cash or as fully paid-up newly issued shares without dealing costs for shareholders. One month later, in June 2012, 4,424,217 new shares were listed for trading with a face value of  $\in$  0.12 each as a remuneration scheme for shareholders.

Therefore, at the 2012 year closing Almirall's share capital totalled  $\in$  20.5 MM, represented by 170,522,827 shares, with a face value of  $\in$  0.12 each, all of which had been fully subscribed and paid up.

For the 2013 AGM, the Board of Directors has agreed to table a motion of a dividend of  $\in$  0.15 gross per share (rounded figure). The scrip dividend scheme will allow shareholders to choose between a cash payout or scrip dividend shares.

## **Shareholders**

According to the information in the official registries of the Spanish Securities Commission, the majority shareholders of Almirall S.A., whether direct or indirect, with a shareholding of over 3 % as at 31 December 2012 were as follows:

For the 2013 AGM, the Board of Directors has agreed to table a motion of a dividend of € 0.15 gross per share (rounded figure)

Name or company of direct shareholders	Number of shares in 2012	Shareholding in Almirall (in %)	
Grupo Plafin S.A.	78,967,993	46.309 %	
Todasa S.A.	43,195,537	25.331 %	
Wellington Management Company LLP	8,365,521	4.905 %	

### Bibliography

- Jones PW, Singh D, Bateman ED, et al. Efficacy and safety of twice-daily aclidinium bromide in COPD patients: the ATTAIN study. Eur Respir J. 2012;Mar 22 [Epub ahead of print].
- Kerwin EM, D'Urzo AD, Gelb AF, Lakkis H, Gil EG, Caracta CF, on behalf of the ACCORD 1 study investigators. Efficacy and safety of a 12-week treatment with twice-daily aclidinium bromide in COPD patients (ACCORD COPD I). COPD. 2012;9:90-101.
- Efficacy of Aclidinium Bromide Compared with Tiotropium and Placebo in Patients with Moderate to Severe COPD: A Phase IIIb Study. Jutta Beier, Anne Marie Kirsten, Robert Mroz, Rosa Segarra, Ferran Chuecos, Cynthia Caracta, Esther Garcia Gil. Thorax 2012; 67: Suppl 2 A26-27.
- 4. Eklira Genuair Summary of Product Characteristics issued by the EMA in July 2012.
- Agusti A, Jones PW, Bateman ED, et al. Improvement in symptoms and rescue medication use with aclidinium bromide in patients with chronic obstructive pulmonary disease: results from ATTAIN. Poster presented at the European Respiratory Society Annual Congress, Amsterdam, The Netherlands, Sept 24-28, 2011.
- Gavaldà A, Miralpeix M, Ramos I, et al. Characterization of aclidinium bromide, a novel inhaled muscarinic antagonist, with long duration of action and a favorable pharmacological profile. JPET. 2009;331(2):740-751.
- Eklira<sup>®</sup> Genuair<sup>®</sup> patient information leaflet issued by the EU in July 2012.
- European Medicines Agency CHMP public summary of opinion. 20 September 2012. EMA/CHMP/604998/2012.
- Rao S, Lembo AJ, Shiff SJ, et al. A 12-week, randomized, controlled trial with a 4-week randomized withdrawal period to evaluate the efficacy and safety of linaclotide in irritable bowel syndrome with constipation. Am J Gastroenterol 2012; 107:1714–1724.
- "European Medicines Agency recommends authorisation of first medicine specifically for irritable bowel syndrome.", European Medicines Agency Press Office, 21 September 2012.EMA/CHMP/611096/2012.
- 11. Quigley EM, Tack J, Chey WD, et al. Randomised clinical trials: linaclotide phase 3 studies in IBS-C - a prespecified further analysis based on European Medicines Agency-specified endpoints. Aliment Pharmacol Ther. 2013 Jan;37(1):49-61.
- 12. Trojano et al., Expert Review of Neurotherapeutics, March 2013, Vol 13, No 3, Suppl 1, pp 1-26.



Almirall, S.A. General Mitre, 151 08022 Barcelona Spain Tel. +34 93 291 30 00 Fax +34 93 291 31 80 www.almirall.com