

# Bringing innovation to global health

Crucell Annual Report and Form 20-F 2009



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### Shareholders' information

Crucell N.V. is a public limited liability company registered in the Netherlands. Crucell's shares are listed on NYSE Euronext (Amsterdam), and SWX Swiss Exchange (Zurich) stock exchanges and Crucell's American Depositary Shares (ADSs) are listed on NASDAQ (New York). The shares listed on NYSE Euronext, as well as the ADSs listed on NASDAQ, are traded under ticker symbol CRXL. The shares trade under ticker symbol CRX at SWX Swiss Exchange. Our website can be found at [www.crucell.com](http://www.crucell.com). This publication comprises the full Annual Report that complies with all applicable Dutch regulations for statutory purposes and the Form 20-F for filing with the Securities and Exchange Commission (SEC) in the US. Cross-references to Form 20-F are set out on pages 236 to 237. The Crucell 2009 Annual Report and Form 20-F (hereinafter referred to as the Annual Report) is prepared in English as approved by the General Meeting of Shareholders and expressed in Euro. All amounts set forth in this Annual Report, unless otherwise noted, are in thousands of Euro, except share and option data.

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Research & development [page 20](#)



Technologies [page 26](#)



Products [page 30](#)

## Our mission

Crucell's mission is to protect human lives from infectious diseases by bringing meaningful innovation to global health.

# €358.0 mln

**Total revenues and other operating income in 2009**

An increase of 26% compared to €283.3 mln in 2008.

# €39.0 mln

**Operating profit in 2009**

Compared to €7.4 mln in 2008.

# €23.9 mln

**Net profit in 2009**

An increase of 68% compared to €14.3 mln in 2008.

## 2009 key highlights

- Record revenues and profits in 2009
- Strategic collaboration Johnson & Johnson
- NIH award for flu-mAbs
- Positive results rabies Phase II Philippines
- Promising preliminary results HIV Phase I
- Collaboration MVI for malaria vaccine
- Exclusive license hepatitis C antibodies
- Total Quinvaxem® contracts \$0.8 billion
- New Korea facility technically complete
- Strengthening vaccine sales in UK
- 12 new license/vendor agreements

## Crucell at a glance



**Crucell is a fully integrated biopharmaceutical company. We focus on developing, producing and marketing products that combat infectious diseases.**

### Who we are

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Crucell is a fully integrated biopharmaceutical company dedicated to bringing meaningful innovation to global health by developing, producing and marketing products to combat infectious diseases. Innovation is the driving force behind our strong research & development (R&D) pipeline, with promising products in pre-clinical and clinical development. Crucell product candidates include flu-mAb, an antibody product effective against a broad range of influenza virus strains, tuberculosis and malaria vaccines, as well as a rabies monoclonal antibody combination—all produced on our unique PER.C6® human cell-line technology.

The sustainability of our business is demonstrated by our solid balance sheet and our strong cash flow. For a company of our size, we invest heavily in R&D: our R&D expenditures in 2009 were €70.2 million.

### Strategy

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We develop products that address currently unmet medical needs, particularly in the field of infectious diseases. We have a fully integrated infrastructure for in-house development, production and marketing of vaccines, and we are leveraging our knowledge in the vaccines field to excel in the antibodies market. Our competitive edge comes from our proprietary technology platforms like PER.C6®, which is ideally suited for the manufacture of vaccines and therapeutic proteins, such as antibodies. Compared to traditional production platforms, PER.C6® technology offers much higher yields at lower cost, as well as safety advantages. The markets we operate in, our technological knowledge and our quality marketed products position us to be a major player in the multi-billion dollar biopharmaceutical arena.



We focus on the paediatric, travel & endemic and respiratory markets. Our core product portfolio includes Quinvaxem®, a fully liquid pentavalent vaccine against five important childhood diseases; Epaxal®, the only aluminum-free hepatitis A vaccine on the market; Vivotif® and Dukoral®, oral vaccines against typhoid and cholera; and Inflexal® V, a virosomal adjuvanted vaccine against influenza. In 2009 we distributed more than 115 million doses of vaccines in over 100 countries, focusing strongly—but not exclusively—on unmet medical needs in developing countries.

#### Partners and licensees

In addition to our own R&D activities, we have strategic partnerships with several leading healthcare companies. Through these agreements, our technologies play a vital role in the development of a vast number of vaccines and antibody products. Some of our partners and licensees are listed below.

- |                     |                  |
|---------------------|------------------|
| • Cangene           | • MedImmune      |
| • Centocor          | • Merck          |
| • CSL               | • Novartis       |
| • DSM Biologics     | • sanofi pasteur |
| • Gedeon Richter    | • Talecris       |
| • GSK               | • TapImmune      |
| • Johnson & Johnson | • Wyeth          |

#### Why infectious diseases?

Infectious diseases currently account for a significant number of human casualties throughout the world. The number of infectious outbreaks is increasing for many reasons: higher population density which raises exposure to infectious agents; an ageing population which is more susceptible to infection; and a rise in global travel which boosts the potential for spreading diseases across borders.



# €304.4 mln

#### Product sales in 2009

Compared to €226.1 mln in 2008.

# €327.8 mln

#### Cash and cash equivalents at year-end 2009

Strong cash position to invest in profitable growth.

# €0.34

#### Net profit per share in 2009

Compared to net profit per share of €0.22 in 2008.

## Crucell: A global perspective

- Marketing & sales
- Manufacturing



## Research & development

### Vaccines in development:

**Flavimun®** yellow fever vaccine.

**Influenza** cell-based seasonal vaccine.<sup>1</sup>

**Tuberculosis** recombinant AdVac®-based vaccine.

**Malaria** recombinant AdVac®-based vaccine.

**Ebola and Marburg** recombinant AdVac®-based vaccine.

**HIV** recombinant AdVac®-based vaccine.

### Human monoclonal antibodies in development:

**Rabies** antibody combination.

**Influenza** antibodies.

**Hepatitis C** antibody combination.

**Details on: p20**

## Technologies

**PER.C6®** human cell line for development and manufacturing.

**AdVac®** used with PER.C6® to develop recombinant vaccines.

**MAbstract®** to discover novel drug targets and identify human monoclonal antibodies.

**STAR®** to enhance yields of recombinant human antibodies and proteins.

**Virosome** a vehicle enabling the use of virus antigens in the making of vaccines.

**Details on: p26**

## Products

### Paediatric:

**Quinvaxem®** fully liquid vaccine to protect against five important childhood diseases.

**Hepavax-Gene®** recombinant hepatitis B vaccine.

**Epaxal® Junior** low dosage, aluminum-free hepatitis A vaccine.

**MoRu-Viraten®** vaccine for protection against measles and rubella.

### Travel & endemic:

**Epaxal®** aluminum-free hepatitis A vaccine.

**Vivotif®** oral typhoid vaccine.

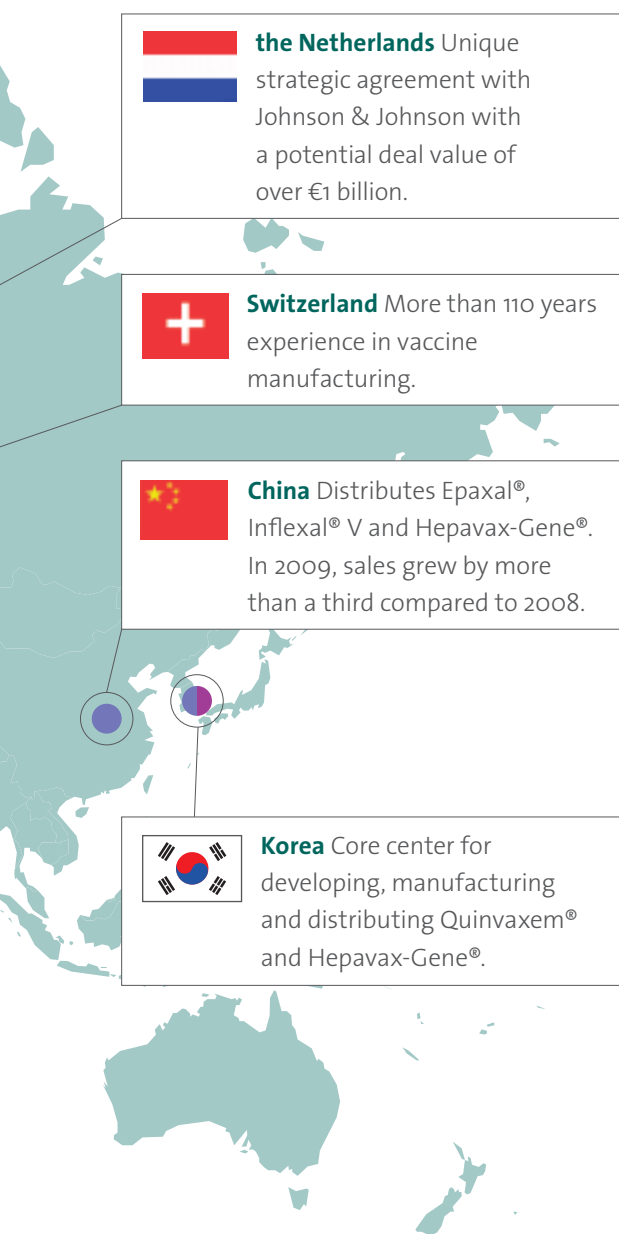
**Dukoral®** only internationally licensed oral vaccine against cholera (and ETEC).

### Respiratory:

**Inflexal® V** virosomal adjuvanted influenza vaccine.

**Details on: p30**

<sup>1</sup> Developed by sanofi pasteur using PER.C6®

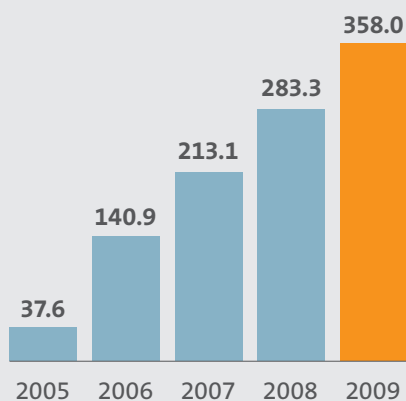


# Performance highlights

## Financials

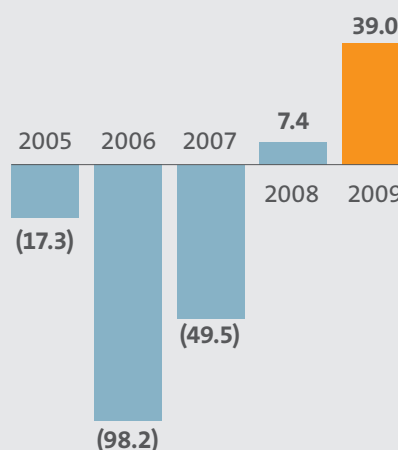
### Total revenues and other operating income

(€ million)



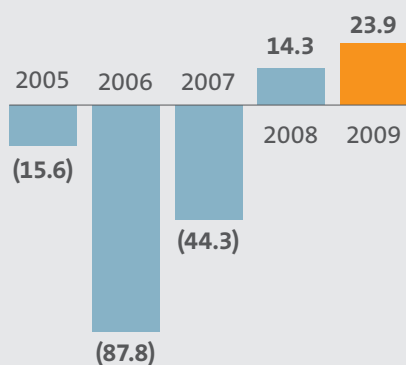
### Operating profit/(loss)

(€ million)



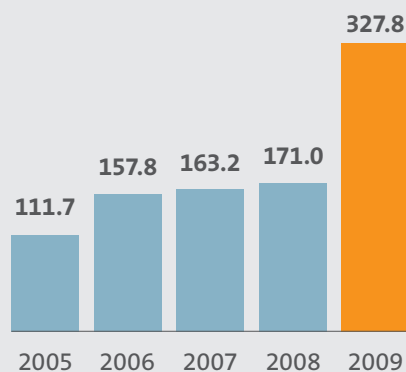
### Profit /(loss) for the period

(€ million)



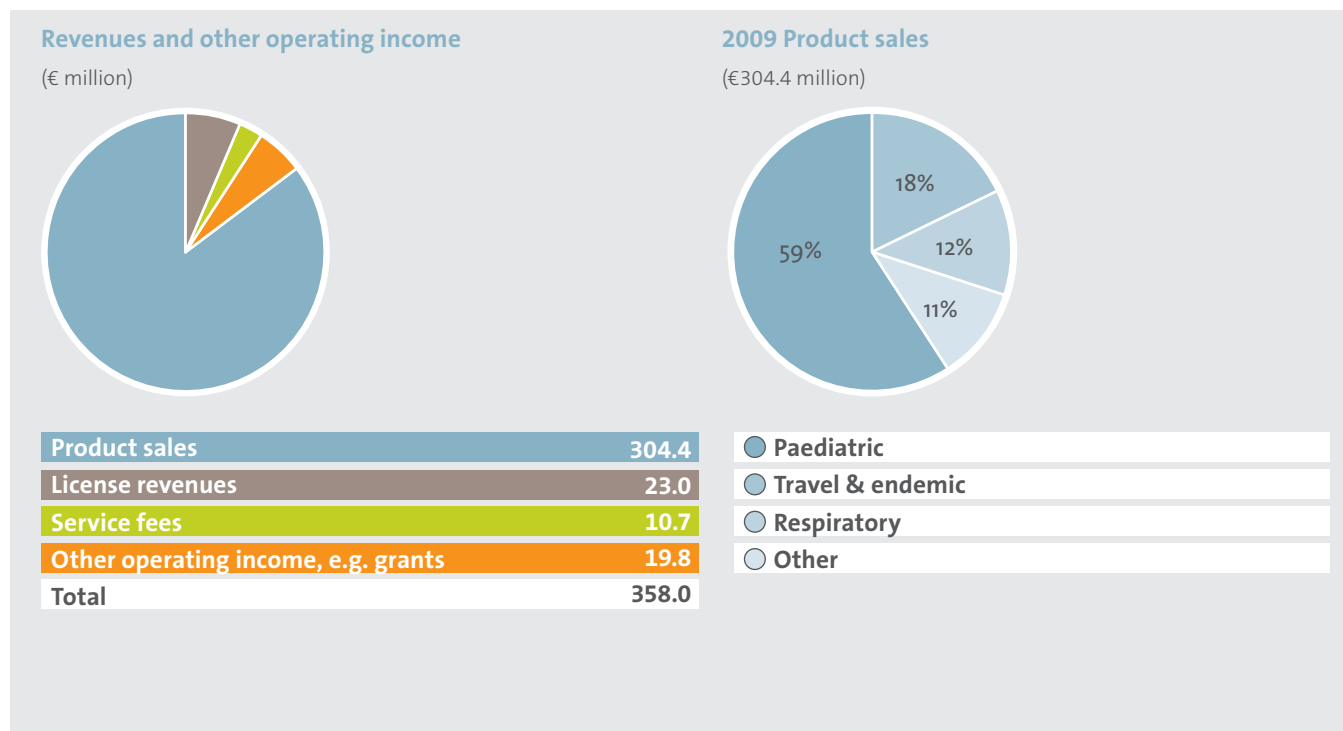
### Cash and cash equivalents at December 31

(€ million)





## Revenues and other operating income



## Outlook for 2010

Use continued strong operating cash flow to accelerate product development.

Research & development spending to increase by over one-third, while maintaining a healthy operating profit.

Revenues and other operating income broadly in line with 2009.<sup>1</sup>

<sup>1</sup> In guidance currency = EUR/USD rate of 1.41.

## Performance highlights continued

### Selected financial data

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Our consolidated financial statements and Company financial statements (hereinafter referred to as the ‘financial statements’), and the notes thereto, have been prepared in accordance with International Financial Reporting Standards (IFRS) as endorsed by the European Union (EU) and as issued by the International Accounting Standards Board (IASB). No differences resulted in our financial statements as a result of the preparation in accordance with IFRS as endorsed by the EU and IFRS as issued by IASB as applied to Crucell.

Prior to 2006, we prepared our financial statements, as included in Form 20-F, in accordance with accounting principles generally accepted in the US (US GAAP), which differs in certain significant respects from, and is not comparable with, IFRS. On December 21, 2007, the SEC approved rule amendments under which Form 20-F, as prepared by Foreign Private Issuers (FPIs), will no longer require reconciliation to US GAAP if the financial statements are prepared in accordance with IFRS as issued by the IASB. This rule is applicable for the 2008 financial year. As a result, we do not provide reconciliation to US GAAP.

The selected financial data should be read in conjunction with ‘Operating and financial review and prospects’ and our financial statements and accompanying notes thereto, included elsewhere in this Annual Report.



The following table shows the selected financial data under IFRS for the years ended December 31, 2005 through 2009.

## IFRS selected financial data

Year ended December 31, (in thousands of Euro, except share data)	2009	2008 <sup>1</sup>	2007 <sup>1</sup>	2006 <sup>1</sup>	2005 <sup>1</sup>
Consolidated statement of income data:					
Revenues:					
Product sales	304,439	226,055	177,569	103,918	—
License revenues	23,049	30,202	12,211	16,955	20,848
Service fees	10,675	10,900	14,006	10,694	11,881
<b>Total revenues</b>	<b>338,163</b>	<b>267,157</b>	<b>203,786</b>	<b>131,567</b>	<b>32,729</b>
Total cost of sales	(194,613)	(145,755)	(134,884)	(90,489)	(7,156)
<b>Gross margin<sup>2</sup></b>	<b>143,550</b>	<b>121,402</b>	<b>68,902</b>	<b>41,078</b>	<b>25,573</b>
Total other operating income	19,839	16,152	9,330	9,356	4,840
Operating expenses:					
Research & development	(70,176)	(70,229)	(63,995)	(67,606)	(34,048)
Selling, general and administrative	(61,400)	(64,778)	(63,566)	(47,478)	(13,689)
Restructuring	—	—	—	(3,120)	—
(Reversal of) impairment	7,199	4,888	(171)	(30,416)	—
Total other operating expenses	(124,377)	(130,119)	(127,732)	(148,620)	(47,737)
<b>Operating profit/(loss)</b>	<b>39,012</b>	<b>7,435</b>	<b>(49,500)</b>	<b>(98,186)</b>	<b>(17,324)</b>
Financial income & expenses	(3,193)	(2,662)	1,378	1,747	2,201
Results non-consolidated companies	2,147	1,442	1,190	(1,956)	(455)
Disposal of subsidiaries	—	(367)	—	—	—
Profit/(loss) before tax	37,966	5,848	(46,932)	(98,395)	(15,578)
Income tax	(14,028)	8,402	2,598	10,611	—
<b>Profit/(loss) for the year</b>	<b>23,938</b>	<b>14,250</b>	<b>(44,334)</b>	<b>(87,784)</b>	<b>(15,578)</b>
Net profit/(loss) per share—basic	0.34	0.22	(0.68)	(1.54)	(0.39)
Net profit/(loss) per share—diluted	0.33	0.21	(0.68)	(1.54)	(0.39)
Weighted average shares outstanding—basic	70,266	65,593	65,103	57,064	39,852
Consolidated statement of financial position data:					
Assets:					
Cash and cash equivalents	327,837	170,969	163,248	157,837	111,734
Total current assets	655,071	322,318	303,262	317,071	131,038
Total assets	1,011,131	636,297	629,838	653,961	169,737
Liabilities and shareholders' equity:					
Total shareholders' equity	738,265	452,534	440,913	497,683	137,609
Total non-current liabilities	114,700	65,462	74,183	66,026	9,380
Total current liabilities	158,166	118,301	114,742	90,252	22,748
Total liabilities and shareholders' equity	1,011,131	636,297	629,838	653,961	169,737
Number of employees	1,248	1,126	1,126	1,073	282

<sup>1</sup> Prior year numbers have been adjusted retrospectively, following the change in accounting policy to recognize actual gains and losses in other comprehensive income.

<sup>2</sup> Gross margin = total revenues less cost of sales.

## Message from our CEO

Ronald H.P. Brus  
(CEO)



In 2009, Crucell's vaccines were administered to a vast number of people worldwide, thereby preventing more than 3.6 million cases of infectious disease and over 819,000 deaths.<sup>1</sup>

### Dear shareholder,

In 2009, we made great strides in terms of global integration, streamlining the way we work, improving performance and increasing accountability—all with the ultimate aim of increasing the impact Crucell has on human health. These achievements form a solid foundation on which to build our future.

Crucell is a rapidly growing biopharmaceutical company with ambitious goals. We aim to create shareholder value by following a clear and convincing strategy for profitable growth by continued innovation. Our core business is stronger than ever and, with a clear strategy for sustainable growth and even more focus on research & development (R&D) activities, we continue to increase the number of people we can protect from illnesses and deaths caused by infectious diseases. I am very proud that for the second year running, we have achieved profitability. Together with solid revenue growth and a very strong year-end cash position, we were able to end 2009 on a high.

In 2009, we distributed more than 115 million vaccine doses in more than 100 countries throughout the world and we were able to take The Crucell Ambition, our corporate strategy for bringing innovation to global health, to the next level. The progress we made in 2009 is a clear indication that we are executing our strategy. Growth is the major theme underlying all our efforts. Our total revenues and other operating income in 2009 increased by 26% compared to 2008 and were driven by strong sales of vaccines.

The pandemic (H1N1) 2009 influenza virus brought into sharp focus the urgency of our mission to develop new solutions for infectious diseases, while making sure that our innovative products already on the market reach all those who need them. The relatively mild, but highly infectious, nature of the virus sparked public discussion about the need for vaccination and the quality of the available vaccines. The revolutionary influenza antibody research going on in our innovation & discovery department is what attracted Johnson & Johnson (JNJ) to sign a truly unique agreement with Crucell in September 2009. This partnership, with a

<sup>1</sup> Figures based on Crucell vaccines Quinvaxem®, Hepavax-Gene®, Inflexal® V, Epaxal® and Vivotif®.

total deal value of over €1 billion, including an upfront payment of over €300 million, comes with exceptional safeguards of Crucell's ongoing independence. The partnership with JNJ is a strong endorsement of Crucell's in-house capabilities for medical innovation and discovery, and a tremendous boost for these capabilities. JNJ's investment in Crucell enables us to accelerate and expand our R&D programs and supports our move into new markets for our existing products. We have a responsibility to make the most of these opportunities.

As we grow further, capturing synergies and rationalization become ever more important. A rigorous review of Crucell's business processes worldwide led to the operational excellence program 'Healthy Ambition', one of the strategic pillars of The Crucell Ambition, which was rolled out in early 2008 and completed in 2009. The program achieved run-rate savings of over €30 million by the end of 2009 and contributed to our positive results through improved yields in our production facilities, savings in overhead and many other operational improvements.

The launch of one global Crucell brand in November 2009 reflects the new maturity of our organization and our growing impact on world health, which further strengthens our ability to bring innovation to global health. The new brand design is one we are proud of. It is strong in its simplicity, with bold use of color and form, and was inspired by the 'eye' of the Crucell logo. The 'eye' is the symbol of our vision as a company founded on innovative technologies and continuously looking for solutions to global health threats.

There is one other innovation I would like to highlight: the progress we are making in adopting a structured approach to corporate social responsibility (CSR). Crucell understands its responsibilities with regard to the environment and strives to be as transparent as possible about its activities. As we build the business, we must never forget to measure our success as a company in human as well as in financial terms. Think of what we can achieve together in 2010 if we all set ourselves the same goal: to make a meaningful difference to Crucell's business, and with that to the health of people around the world. See pages 34-71 for more information on our CSR activities.

## “Long-term growth is the major theme underlying all our efforts.”

On June 25, 2009, I celebrated 12.5 years with Crucell —a milestone anniversary in Dutch culture. Like most anniversaries, this one got me thinking about both the past and the future. Over the years, I have seen Crucell grow from a small biotech start-up to a global organization that is making a real difference to the health of people worldwide. That was my dream when I started at Crucell and I am both proud and grateful that, together with more than 1200 highly qualified and dedicated colleagues, we have made it a reality. More importantly, I see that we are expanding the boundaries of that reality, day by day. Innovation is the foundation on which Crucell was built, and what gives us the momentum to move forward.

Our achievements so far are thanks to the tireless efforts and motivation of our employees, Crucell's most important asset, and to your willingness as a shareholder to invest in Crucell. For 2010, we foresee another good year for Crucell and we thank you for your continued support.



**Ronald H.P. Brus**

President and Chief Executive Officer  
Leiden, the Netherlands, April 6, 2010

# The Crucell Ambition

Here at Crucell, each innovation, business decision and new development is driven by one single aim—our desire to improve healthcare across the globe.

To support this vision, we developed The Crucell Ambition, a global corporate strategy encompassing coordinated efforts in four priority areas—Organization & People, Focus, Operational Excellence and Deliver on Promises.

The Crucell Ambition was rolled out worldwide in 2008, and in 2009 it proved to be a great success, realizing just over €30 million in run-rate savings and moving us another step closer to becoming one global Crucell.

Below are just a few examples of how The Crucell Ambition has been embraced by employees and translated into visible results.

## New business model

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A new business model was presented company wide. This transformed Crucell from a vertically organized company, where interrelated functions were fragmented and efficiency, speed and long-term planning were affected, into a global business run along horizontal lines. Three cross-functional business franchises were introduced for paediatric, travel & endemic and respiratory products.

**“It is a real pleasure to work in this manner.”**

Each business franchise has an overall business manager responsible for optimizing the profitability of the business across all functions: innovation & discovery, development, operations and marketing & sales. Four value streams, which are dedicated to different products, or products with similar manufacturing processes, have also been established. This allows us to streamline processes and focus on continuous improvement.



## Information management

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Alongside the demands of their usual roles at Crucell, many employees have been working hard on developing a global system for information management: an enterprise resource platform (ERP). Thanks to their dedication, it is on schedule and many facets will be rolled out in 2010. A welcome by-product of the project is the great team spirit created within the cross-functional teams drawn from Crucell sites around the world.

**“The Crucell Ambition is a good way to improve and make Crucell a better company for tomorrow.”**

## One global identity

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Crucell's new global brand was born in November 2009. Following a smooth launch, implementation of the brand began at all Crucell sites except the Korean site, where the rebranding is being timed to correspond with the move to the new manufacturing facility being built in the Incheon Free Economic Zone. The new brand marks the successful integration of various Crucell companies and displays our commitment to being a leading biopharmaceutical company.



## Manufacturing revolution

Crucell's process development team has revolutionized its manufacturing facilities with the creation of the 'FlexFactory®', utilizing mobile manufacturing equipment in a mobile clean room. This development will lead to significant financial and environmental savings for Crucell. For more information see page 45.

**“This is a clear strategy and provides a sound foundation for us to build on.”**

## Corporate social responsibility

Our commitment to corporate social responsibility (CSR) led to a number of exciting developments for Crucell in 2009. We acted on our desire to focus more on CSR performance and transparency and implemented a strategy for how to do this. See pages 34-71 for more information on our CSR program.

The Crucell Ambition strategy breathes life into the Crucell Values, a set of guiding principles adopted by our employees. These values allow us to cultivate the kind of qualities within our company that help us realize even the most ambitious goals, and are a strong unifying force within Crucell.

**“The positive results achieved are the best efficiency statement for The Crucell Ambition program—let's carry on!”**

## Crucell Values



The image above highlights the Crucell Values in the many languages spoken by Crucell employees around the world.

Quotes: Crucell employees' views on The Crucell Ambition.

# Management Committee

## Crucell has a two-tiered board structure in which executive and supervisory responsibilities are clearly separated.

The Supervisory Board is comprised of independent, non-executive individuals who are charged with supervising and advising Crucell's Management Board. The Management Board, which is a subset of the Management Committee, is responsible for the general affairs and business of the company and, as such, is responsible for achieving Crucell's goals, strategy and policy, as well as results.

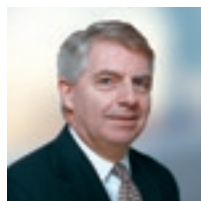
### **Dr. Ronald Brus (1963)\*** **President and Chief Executive Officer**



Dr. Ronald Brus is Crucell's President and Chief Executive Officer. He has been a member of Crucell's Management Committee since the company's incorporation and was formerly Chief Operating Officer (March 2003 to January 2004) and

Chief Business Officer (October 2000 to February 2003). Prior to that, he was Executive Vice President for Business Development when he joined the company in 1997. From 1994 to 1996 he was product planning physician at Forest Laboratories in New York and from 1990 to 1994 he was Medical Director for Zambon B.V. He holds a medical degree from the University of Groningen, the Netherlands. Dr. Brus is Chairman of the Management Board.

### **Leonard Kruimer (1958)\*** **Chief Financial Officer**



Mr. Leonard Kruimer has been Chief Financial Officer since he joined Crucell in 1998 and is a member of Crucell's Management Board and Management Committee. Prior to Crucell, he held interim executive positions at Pepsico and Royal Boskalis Westminster. From

1993 to 1995, he was Managing Director for Continental Europe at TIP Europe, a unit of GE Capital. Prior to that he held senior executive positions at Kwik-Fit Europe and Continental Can Europe. He was a consultant with McKinsey & Co and started his career at PriceWaterhouse & Co in New York. He holds an MBA from the Harvard Graduate School of Business Administration and an undergraduate degree from the University of Massachusetts. He is a CPA in New York State.

### **Dr. Cees de Jong (1961)\*** **Chief Operating Officer**



Dr. Cees de Jong joined Crucell as Chief Operating Officer in September 2007. He became a member of Crucell's Management Board in May 2008. Prior to that he worked at Quest International in Naarden, the Netherlands, as a member of the

Board responsible for the Flavours Division. Prior to Quest, he worked as Managing Director of DSM Anti-infectives. In 1989, he started his career at Gist Brocades, holding a variety of roles in Business Development, Strategy and General Management before the company's acquisition by DSM in 1998. He holds a medical degree and earned an MBA at the Erasmus University Rotterdam, the Netherlands.

**Dr. Jaap Goudsmit (1951)\***  
**Chief Scientific Officer**

Dr. Jaap Goudsmit is Crucell's Chief Scientific Officer and is responsible for all R&D activities. He became a member of Crucell's Management Board in January 2004. He joined Crucell in 2001 as Senior Vice President for Vaccine Research and

became a member of Crucell's Management Committee in July 2002. Prior to that, he held various positions at the Academic Medical Center at the University of Amsterdam and was Chairman of the Research Institute for Infectious Diseases and the Institute for Science Education. Since 1989, he has been a professor at the University of Amsterdam and the Academic Medical Center. He holds a medical degree and a PhD from the University of Amsterdam, the Netherlands.

**René Beukema (1964)**  
**General Counsel and Corporate Secretary**

Mr. René Beukema has been Crucell's General Counsel and Corporate Secretary since the company's incorporation. He held the same position at IntroGene after joining the company in 1999. From 1994 to 1999, he was Senior Legal Counsel for GE

Capital/TIP Europe. From 1991 to 1994, he was Legal Counsel for TNT Express Worldwide N.V. He has a Masters in Law from the University of Amsterdam, the Netherlands.

**Arthur Lahr (1968)**  
**Chief Strategy Officer and  
Executive Vice President Business Development**

Mr. Arthur Lahr is Crucell's Chief Strategy Officer and Executive Vice President for Business Development. He joined Crucell in April 2001 as Executive Director for Business Development and became a member of the Management Committee in

January 2004, Executive Vice President in January 2006 and assumed responsibility for European Marketing & Sales and Company Strategy in 2006. From 1994 to 2001, he was a consultant with McKinsey & Co. in the Netherlands and New York. Prior to that, he worked at Unilever. He holds a Masters in Business Administration from INSEAD and a Masters in Science in Applied Physics from the University of Delft, the Netherlands.

*Full details of the Management Committee can be found on page 141.*

\* Member of the Management Board.

# Report of the Supervisory Board



Jan P. Oosterveld  
(Chairman)

## Dear shareholder,

The Supervisory Board is pleased to submit to you the combined Annual Report and Form 20-F, including the financial statements of Crucell N.V. for the year ended December 31, 2009, as prepared by the Management Board.

Attached to the financial statements is the auditor's report by Deloitte Accountants B.V., free from any qualification. We adopted the financial statements for the year 2009 and advise the General Meeting of Shareholders to approve these statements and to grant discharge to the Management Board, with respect to its management and to the Supervisory Board, with respect to its supervision.

The Supervisory Board held thirteen meetings with the Management Board in 2009, of which eight were in the form of conference calls. The meetings were arranged in such a way that, on several occasions, the Supervisory Board could meet immediately after the departure of the Management Board; so called closed sessions. There were also a number of more informal contacts between Supervisory Board Members and the Management Board.

The Supervisory Board was closely involved in all developments affecting the Company in terms of strategy, tactics and operations in the financial year 2009. The Board's meeting schedule not only reflects its commitment to the Company's affairs, but also the dynamic way in which the Company is rapidly consolidating its position in the biotech industry. Thanks to the well-documented information provided by, and to, the frequent discussions with the Management Board, the Supervisory Board was able to acquire a comprehensive perspective on all aspects of the Company's strategy. Where Supervisory Board approval of proposals was required, it was able to arrive at decisions based on solid facts and coherent arguments.

All Supervisory Board meetings and conference calls were well attended. Regular items on the agenda included the Company's financial performance, based on quarterly

reports, its budget and its business, including the research & development (R&D) portfolio, intellectual property matters and operational updates. Importantly, the Board also discussed the Company's strategy and its near-, mid- and long-term risks, the current and future strategic objectives, planned acquisitions, the Johnson & Johnson (JNJ) strategic collaboration, sanofi pasteur and DSM collaborations and the reports from the Audit Committee, the Remuneration Committee, Research & Development Committee and Nomination Committee. Other significant issues addressed were compliance with Section 404 of the American Sarbanes-Oxley Act of 2002 and related regulations (SOX 404), the ongoing corporate rationalization processes and the progress made in integrating acquired businesses.

The Supervisory Board also discussed its own performance, reviewing its function and its individual members, and the performance of the Management Board and its individual members. The design of the strategic collaboration between Crucell and JNJ was discussed frequently and in detail with the Management Board and its financial advisors. In particular, the legal and financial consequences of such strategic collaboration were reviewed with Crucell's in-house and outside legal advisors.

In order to make decisions, the Supervisory Board has established an Audit Committee, a Remuneration Committee, a Nomination Committee and a Scientific Committee. For detailed information on the composition and activities of these committees, please see 'Corporate Governance—Supervisory Board'.

In 2009, the Audit Committee met nine times, of which four were conference calls. The Company's external auditor, Deloitte Accountants B.V., routinely attended these meetings, in particular, where the annual accounts, the auditor's report and the quarterly results were discussed.

Deloitte has been Crucell's external auditor since 2006. The performance of Deloitte will be evaluated by the Audit Committee, which will present its findings to the full Supervisory Board.



Steve Davis



Arnold Hoevenaars



Seán Lance



Phillip Satow



Floris Waller



Claes Wilhelmsson

The Nomination Committee consists of the full Supervisory Board and, as such, met four times during the 2009 fiscal year to discuss the Supervisory Board's composition and functioning. The Scientific Advisory Committee held two meetings with R&D management to discuss issues around protein production and various infectious diseases. They also covered R&D budgets and organizational matters.

The Remuneration Committee met four times to review collective 2009 milestones and set objectives for 2010, to approve and ratify option grants and to discuss the remuneration policy for the second and third tiers of management. The Remuneration Committee and the Supervisory Board operate within the framework of the remuneration policy for the Management Board, which was amended and adopted by the Annual General Meeting of Shareholders in June 2009 and remains unchanged. The remuneration of the Management Board members is determined by the Supervisory Board, based on a proposal by the Remuneration Committee. It conforms to market practice and is aimed at attracting qualified and expert management with the skills required to run a publicly listed company active in the pharmaceutical industry.

The remuneration of members of the Supervisory Board complies with almost all aspects of the provisions of the Dutch Corporate Governance Code. The exceptions are where it conforms more closely to customary practice in the biotechnology industry worldwide. These exemptions are disclosed in the section 'Corporate Governance—Exceptions to Compliance with the Code'.

The compensation of all Supervisory Board members consists of a fixed fee in cash and an annual share grant. Instead of the share grant, a Supervisory Board member may instead choose to receive a cash amount equaling the value of the share grant, minus a discount.

The remuneration of the Supervisory Board is further detailed in the corporate governance section of our management report. The remuneration policy can be found on Crucell's website ([www.crucell.com](http://www.crucell.com)), which is not incorporated by reference herein.

The Nomination Committee initiated a global search to fill a vacancy on the Supervisory Board. As a result, and after careful consideration, the Supervisory Board is pleased to report that Floris Waller was elected in June 2009 to the Supervisory Board.

The members of the Supervisory Board would like to thank the Management Board, the Management Committee, senior management and all employees for their devotion, their motivation and their loyalty in a year in which we continued to show significant growth and took further strides toward realizing Crucell's ambitious aspirations.

In particular, we would also very much like to thank our shareholders for their continued support and dialogue.

**Jan P. Oosterveld**

Chairman of the Supervisory Board  
Leiden, the Netherlands, April 6, 2010



## Research & development, technologies and products



Research & development



Technologies



Products

We develop, produce and market vaccines and antibodies against a range of infectious diseases, focusing strongly—but not exclusively—on unmet medical needs in developing countries and emerging economies. Vaccines play a vital role in protecting against diseases and have contributed significantly to the improvement of global public health in the 21st century. In the following pages we highlight Crucell's key innovations.

# €358.0 mln

**Total revenues and operating income**

Products continue to show strong growth.

# 115+ mln

Vaccine doses distributed in 2009.

# 100 countries

Crucell vaccines were sold in more than 100 countries in 2009.



Development stage	Research/ Pre-clinical	Phase I	Phase II	Phase III	Marketed	Description
<b>Marketed products:</b>						
Quinvaxem®						Fully liquid vaccine for protection against five childhood diseases.
Hepavax-Gene®						Recombinant hepatitis B vaccine.
Epaxal® Junior						Low dosage, aluminum-free hepatitis A vaccine (0.25ml).
MoRu-Viraten®						Vaccine for protection against measles and rubella.
Epaxal®						Aluminum-free hepatitis A vaccine.
Vivotif®						Oral typhoid vaccine.
Dukoral®						Only internationally licensed oral vaccine against cholera (and ETEC).
Inflexal® V						Virosomal adjuvanted influenza vaccine.
<b>Vaccines in development:</b>						
Flavimun®						Yellow fever vaccine.
Influenza seasonal (flu cell)						Seasonal influenza vaccine. <sup>1</sup>
Tuberculosis						Recombinant AdVac®-based tuberculosis vaccine. <sup>2</sup>
Malaria						Recombinant AdVac®-based malaria vaccine. <sup>3</sup>
Ebola and Marburg						Recombinant AdVac®-based Ebola and Marburg vaccine. <sup>3</sup>
HIV						Recombinant AdVac®-based vaccine. <sup>4</sup>
<b>Human monoclonal antibodies in development:</b>						
Rabies antibody combination						Two human monoclonal antibodies for post-exposure treatment of rabies. <sup>5</sup>
Influenza antibodies						Neutralizing antibody cross reactive against different influenza subtypes including H5 and H1.
Hepatitis C antibody combination						Neutralizing monoclonal antibodies across all genotypes tested.

<sup>1</sup> Developed by sanofi pasteur using PER.C6®. <sup>2</sup> Partnered with Aeras. <sup>3</sup> Partnered with NIH/NIAID. <sup>4</sup> Partnered with Harvard. <sup>5</sup> Partnered with sanofi pasteur.

## Research & development



Our research efforts are bolstered by our technology range, which plays a critical role in our development programs. In the following pages we discuss important developments relating to our discovery programs and highlight our key areas of focus.

**Flavimun<sup>®</sup>** yellow fever vaccine. **Influenza**  
cell-based seasonal vaccine.<sup>1</sup> **Tuberculosis**  
recombinant AdVac<sup>®</sup>–based vaccine.  
**Malaria** recombinant AdVac<sup>®</sup>–based vaccine.  
**Ebola and Marburg** recombinant  
AdVac<sup>®</sup>–based vaccine. **HIV** recombinant  
AdVac<sup>®</sup>–based vaccine. **Rabies** antibody  
combination. **Influenza** antibodies.  
**Hepatitis C** antibody combination.

<sup>1</sup> Developed by sanofi pasteur using PER.C6<sup>®</sup>.

## Research & development continued

We have a strong research & development (R&D) pipeline with promising investigational products.

### Vaccines based on the AdVac® technology

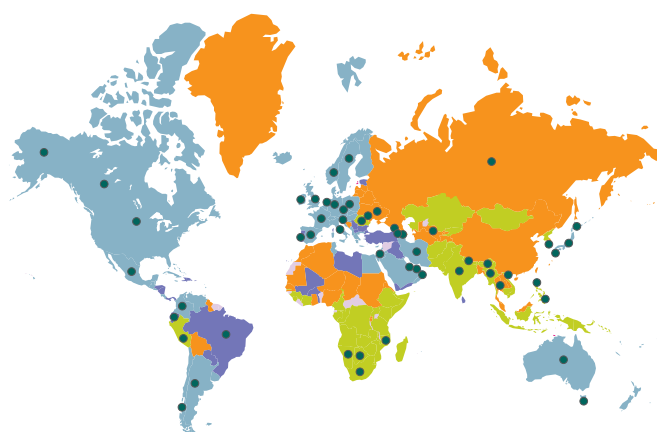
AdVac® technology involves the use of adenoviral vectors, such as Ad35 and Ad26, in vaccines for diseases caused by viruses, bacteria or parasites. These vectors are harmless adenoviruses that have been disabled so that they cannot replicate. A vector functions as an efficient 'gene taxi', delivering into the human body a fragment of DNA that carries the code for a protein of a specific pathogen. Once inside the body, the vectors express (produce) these proteins and present them to the person's immune system, which augments its protective response. Using this versatile vaccine vector platform in combination with our PER.C6® manufacturing technology, we are working with our partners to develop vaccines against diseases like tuberculosis, malaria, Ebola and Marburg and HIV.

### Tuberculosis

Tuberculosis (TB) is a major cause of illness and mortality worldwide, responsible for 9.4 million new cases and 1.8 million deaths in 2008<sup>1</sup>. The current TB vaccine Baccille Calmette Guérin (BCG), developed more than 85 years ago, is probably the world's most widely used but least effective vaccine. It does reduce the risk of disseminated TB, a form that spreads from the lungs to other organs, and is especially lethal in children. However, it does not reliably prevent pulmonary TB, the most prevalent form of the disease. The problem is compounded by the emergence of extensively drug-resistant tuberculosis (XDR-TB).

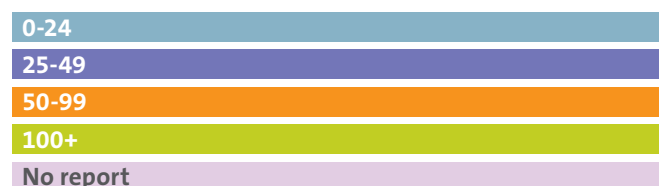
To address this urgent need, Crucell has joined forces with the Aeras Global TB Vaccine Foundation, one of several non-governmental organizations we collaborate with to combat diseases. Together, we are developing the novel TB vaccine candidate AERAS-402/Crucell Ad35.

<sup>1</sup> World Health Organization (WHO) 2009 Update, Tuberculosis Facts.



### Tuberculosis

Notified TB cases (new and relapse) per 100,000 population in 2007.



● Countries that had reported at least one case of XDR-TB by the end of 2008.

(WHO, 2009, Global tuberculosis control)

## Tuberculosis is a leading killer of people with HIV.

(WHO, 2009 Update, Tuberculosis Facts)

Several Phase I trials have been held with promising results—a South African study found that CD8-cell immune responses were much higher than those seen in humans in any previous TB vaccine studies. In January 2010, a Phase I clinical trial was initiated in Portland, Oregon, to obtain a more detailed analysis of the immune response to AERAS- 402/Crucell Ad35. In October 2008, enrollment for the first Phase II study of this vaccine candidate began in South Africa, conducted by the University of Cape Town Lung Institute in conjunction with the South African Tuberculosis Vaccine Initiative. It has found that CD8-cell immune responses are induced in patients who have completed TB treatment.

## More than 2 billion people, equal to one-third of the world's population, are infected with TB bacilli, the microbes that cause TB.

(WHO, 2009 Update, Tuberculosis Facts)

### Malaria

Malaria is one of the most prevalent infections in tropical and subtropical regions with children and pregnant women most severely affected. According to the World Health Organization (WHO), half of the world's population is at risk of malaria, and an estimated 243 million cases led to nearly 900,000 deaths in 2008. No licensed vaccine is currently available.

Crucell is collaborating with the US National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH), on malaria vaccine research and development. A candidate vaccine arising from this partnership is being tested in a Phase I trial at two US sites: Vanderbilt University in Nashville, Tennessee, and Stanford University in Palo Alto, California. Boost vaccinations for the fourth and final group of volunteers have been completed and preliminary examination of the blinded data indicates that the vaccine is immunogenic.

In July 2009, we announced a new collaboration with the US-based Malaria Vaccine Initiative (MVI) and USAID Malaria Vaccine Development Program (MVDP) to accelerate development of a promising new type of malaria vaccine. Using funding from the USAID MVDP, the partners will conduct studies to determine how effectively Crucell's proprietary recombinant adenoviruses (a type of virus associated with the common cold and other mild respiratory infections) delivers a malaria antigen to the immune system. Using Crucell's AdVac® technology with two different adenovirus vectors—Ad35 and Ad26—as delivery mechanisms, this approach seeks to elicit a protective immune response.

### Ebola and Marburg

Ebola is one of the world's most lethal viral diseases and can be found on the US Department of Defense's Category 'A' list of bioterror agents. Both Ebola and Marburg are among the few viruses capable of causing hemorrhagic fever, a severe, often fatal disease in humans. There are currently no vaccines or antiviral therapies available for either disease.

Crucell is developing a multivalent filovirus vaccine against Ebola and Marburg in collaboration with the Vaccine Research Center of the NIH/NIAID. The candidate vaccine is based on Crucell's proprietary adenoviral vector technology and is produced using Crucell's PER.C6® technology.

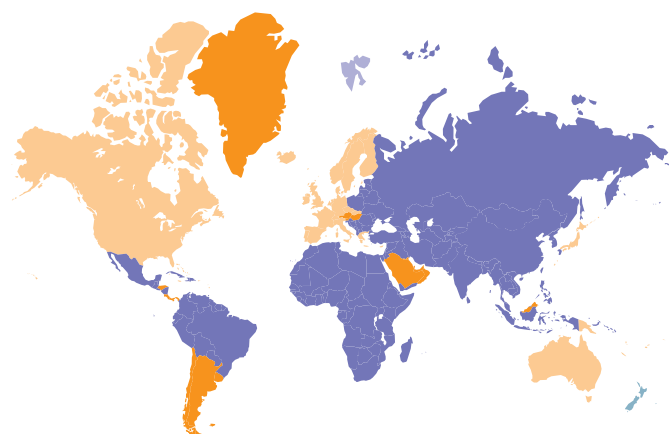
A Phase I study showed safety and immunogenicity at the doses evaluated. Based on these results, a second Phase I study is anticipated. This will use alternative multivalent adenovirus vectors that are able to bypass pre-existing immunity against the more commonly used adenovirus serotype 5 (Ad5).

### HIV

Over the past 25 years, HIV infection resulting in AIDS has claimed millions of lives, devastated communities, and enormously frustrated efforts to fight poverty, improve global health and promote economic development. According to the 2009 AIDS Epidemic Update (a joint report by the United Nations Program on HIV/AIDS (UNAIDS) and WHO), 33.4 million people, more than ever before, are living with HIV. There is currently no licensed HIV vaccine available.

With the support of a \$19.2 million grant from the NIH, Crucell is collaborating with Harvard Medical School and its teaching hospital Beth Israel Deaconess Medical Center to develop a recombinant AdVac®-based vaccine against HIV. Adenovirus serotype 26 (Ad26) is being used as the vaccine vector, in order to avoid the problem of pre-existing immunity to Ad5. Preliminary results of a Phase I study at the Brigham and Women's Hospital in Boston, USA, show that the HIV candidate vaccine is safe and immunogenic.

## Research & development continued



### Antibodies

Antibodies are proteins made naturally by cells of the body's immune system. They function as one of the body's principal defense mechanisms against pathogens – disease-causing agents such as parasites, viruses or bacteria. As antibodies recognize and bind to invading pathogens, ultimately eliminating them, they play a crucial role in protecting humans against disease.

### Rabies antibody combination

Rabies is widespread across the globe. More than 55,000 people die of rabies each year, with around 95% of those deaths occurring in Asia and Africa—usually following a bite from an infected dog.

**Rabies causes more than 55,000 deaths each year in endemic countries.**

(WHO, rabies factsheet, December 2008)

This highlights the significant unmet medical need for a safe, effective and affordable rabies treatment. The treatment currently used when someone is exposed to the virus combines immunoglobulins (antibodies prepared from human or equine blood) with the vaccine. This is usually successful if administered within 24-48 hours

### Rabies

Countries or areas at risk.

No risk
Low risk
Medium risk
High risk
No data available

(WHO, Rabnet/CDC, 2008)

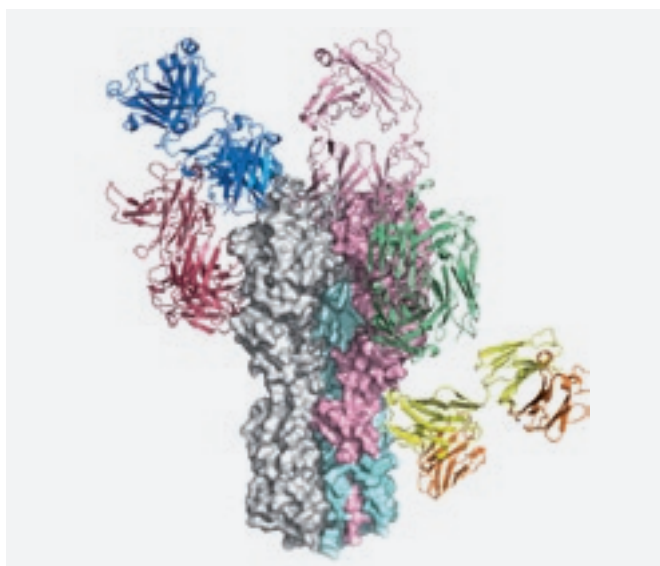
following exposure. However, concerns about the safety and availability of blood-derived rabies antibodies have inspired a search for alternatives.

Using MAbstract® and PER.C6® technology, Crucell scientists—in collaboration with the Thomas Jefferson University in Philadelphia and the US Centers for Disease Control and Prevention in Atlanta—have discovered a combination of human monoclonal antibodies (mAbs) for the post-exposure treatment of rabies. Clinical testing of this mAb combination made good progress during 2008, leading to the presentation in October of very promising efficacy and safety data from a Phase II trial in the US. In order to test the mAb combination in different populations and settings, an additional Phase II trial was held among children in the Philippines, which showed that neutralizing activity levels were similar to those achieved by administering human immunoglobulin (HRIG). A third Phase II study, at Lotus Laboratories in Bangalore, India, is due to begin in the coming months. Since January 2008, the route towards global availability of this next-generation, life-saving rabies biological has been facilitated by Crucell's strategic partnership with sanofi pasteur, a world leader in rabies immunization. The US Food and Drug Administration (FDA) has granted Crucell's mAb combination Fast Track status, paving the way for priority handling of the regulatory dossier.

### Human monoclonal antibodies against a broad range of influenza strains

In December 2008, Crucell announced the discovery of a new class of human monoclonal antibodies (mAbs) with the unprecedented ability to combat a broad range of influenza virus strains.





The broadly neutralizing CR6261 antibody binds in the HA stem, distant from other strain-specific antibodies, by using only its heavy chain.

In a pre-clinical study, Crucell's mAb CR6261 was compared with the anti-influenza drug oseltamivir (Tamiflu) in terms of its value for flu prevention and treatment; the monoclonal antibody strongly outperformed oseltamivir.

The flu strains tested included the 'bird flu' strain H5N1, which experts fear has the potential to cause a pandemic, and H1N1 (including the recent pandemic H1N1 2009 virus), which is similar to a descendant of the flu virus that caused the devastating pandemic in 1918. Importantly, the study showed that CR6261 provides immediate protection against the influenza virus, suggesting that it will be able to prevent disease spread. In contrast, oseltamivir was less efficacious and, in some cases, not effective at all.

In August 2009, Crucell received an award from the US National Institute of Allergy and Infectious Diseases (NIAID), part of the National Institutes of Health (NIH) for the development of our monoclonal antibodies for the treatment of seasonal and pandemic influenza. A month later, Crucell entered into an exciting strategic collaboration with Johnson & Johnson, through its subsidiary Ortho-McNeil-Janssen Pharmaceuticals, Inc. The immediate focus of the collaboration will be the development and commercialization of a universal monoclonal antibody product (flu-mAb) for the treatment and prevention of influenza. One of the key focus areas of the long-term

innovation collaboration will be new discovery programs leading to the development and commercialization of a universal influenza vaccine.

### Hepatitis C antibody combination

In August 2009, Crucell obtained an exclusive license from Stanford University (Palo Alto, California) for the development of an antibody combination against the hepatitis C virus (HCV). A large panel of fully human monoclonal antibodies against HCV is being evaluated by Crucell in a proof of concept phase. The monoclonal antibodies have been found to neutralize the virus across all genotypes tested and each recognizes a different part of the HCV surface protein.



**Worldwide, annual influenza epidemics result in about three to five million cases of severe illness, and about 250,000 to 500,000 deaths.**

(WHO, Influenza (seasonal) fact sheet, April 2009)

# Technologies



Our strong product portfolio is supported by a range of patented technologies. Our cutting-edge technology platforms enable the discovery, development and production of vaccines, therapeutic proteins and gene therapy products.

**PER.C6<sup>®</sup>** a human cell line for development and large-scale manufacturing of biopharma products. **AdVac<sup>®</sup>** used in combination with PER.C6<sup>®</sup> to develop recombinant vaccines. **MAbstract<sup>®</sup>** applied for discovery of novel drug targets and identification of human monoclonal antibodies. **STAR<sup>®</sup>** designed to enhance production yields of recombinant human monoclonal antibodies and proteins. **Virosome** a vehicle enabling the use of virus antigens in the making of vaccines.

## Technologies continued

Crucell's innovative approach has not only led to a broad range of successful vaccines and promising pipeline products, it has also inspired the development of an array of patented technologies to support that portfolio. We have five core proprietary technology platforms.

### PER.C6® technology

Crucell's PER.C6® cell line is derived from a single, human cell, immortalized using recombinant DNA technology. As a result, PER.C6® cells can replicate indefinitely, making them uniquely flexible and ideally placed to meet the rising volume demands and stringent safety requirements of today's biopharmaceutical industry.

In areas where we do not aim to develop our own products, Crucell licenses the technology, leading to a number of companies and organizations around the world opting to use our PER.C6® technology platform. Potential customers not only need our know-how, but our PER.C6® cells, which are only available from us under agreement. This combination ensures PER.C6® is the best protected human cell technology in the world.

# 27 g/L

**Record-level titer achieved at harvest for an antibody product using PER.C6® human cell line technology.**

Since 2008, we have collaborated with DSM Biologics and together we license PER.C6® for proteins and antibodies and invest in further innovation of the technology. We feel there is still tremendous potential to reduce the production costs of monoclonal antibodies whilst increasing yield, leading to more affordable treatments for patients.



**We have developed an enhanced cell settling technique for clarification of high-density cell cultures of PER.C6® cells.<sup>1</sup> The method overcomes the limitations of traditional technologies and provides rapid reduction of cell mass while significantly reducing impurities.**

<sup>1</sup>Emily Schirmer et. al. Bioprocess International, January 2010-02-08.

We also believe that antibody and other protein products based on PER.C6® technology may demonstrate enhanced biological properties, rendering them potentially more effective.

### AdVac® technology

Crucell has been a key player in the development of adenoviral-based vaccines for more than six years. This has led to the availability of proprietary AdVac® vectors, constructed from adenoviruses not usually found

in humans, such as Ad35. AdVac® vectors can be engineered to contain small genetic fragments of various viruses, parasites and bacteria, allowing the development of a wide variety of novel vaccines. While no adenovirus-based recombinant vaccines are currently on the market, AdVac®-based vaccines for tuberculosis (TB), malaria, Ebola and Marburg, and HIV are in (pre) clinical trials.

In contrast to commonly used adenoviral vectors, AdVac® technology can circumvent pre-existing immunity offering accurate dose control of vaccines.

AdVac® vectors can be produced on the PER.C6® cell line, which supports the cost-effective production of industrial-scale quantities of vaccines.

### **MAbstract® technology**

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Our MAbstract® technology selects antibodies for possible therapeutic use and discovers novel drug targets using whole cells, tissues or infectious agents.

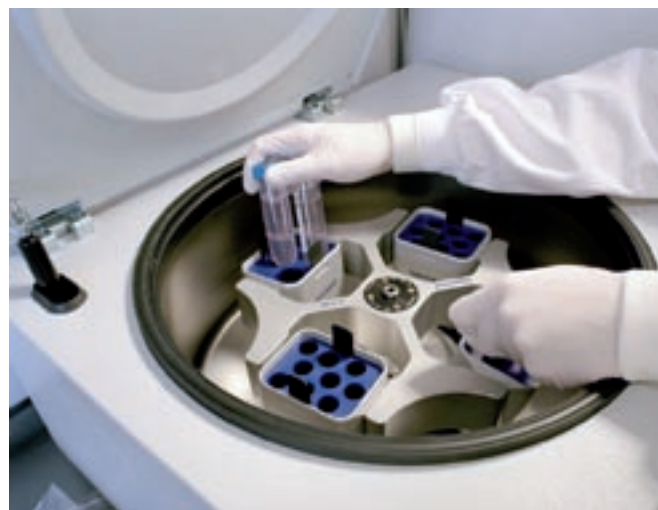
It has been used to isolate antibodies for numerous diseases which can then be directly reformatted into antibodies for production using our PER.C6® technology.

We believe MAbstract® has a number of potential advantages over other technologies on the market. For example, it uses a subtraction method of selection not available when generating human monoclonal antibodies with other technologies and it does not have an inherent limitation on antibody specificity. Fully human monoclonal antibodies also have an excellent safety profile.

### **STAR® technology**

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We acquired STAR® technology in 2004 and it has proved invaluable for increasing production of recombinant antibodies and therapeutic proteins on mammalian cell lines. One of its strong advantages is that the well-established mammalian cell banks used in STAR® technology eliminate the need for specially engineered mammalian cells. This also allows for rapid, stable mammalian cell clone generation, which typically produces five to ten times more antibody or other therapeutic proteins compared to cell clones generated without STAR®.



### **Virosome technology**

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One of the challenges in vaccine development is creating products with defined antigens of high purity that can efficiently induce a protective immune response. To solve this, many antigen preparations resort to adjuvants to enhance the body's immune response. The most commonly used are aluminum salt derivatives, which are known to cause adverse reactions, for example, irritation and inflammation at the injection site.

Our virosome technology offers a tool for developing novel, predominantly synthetic vaccines for infectious and chronic diseases. These vaccines offer additional benefits because they are effective even in immune-suppressed patients and infants.

Virosomes are completely biodegradable and the technology is used in the manufacture of several of Crucell's registered products where it has an excellent safety record.



# Products



Crucell vaccines have an excellent safety record and are distributed globally in more than 100 countries. In the following pages we focus on our range of marketed products, many of which offer unique advantages to the people who benefit from them.



**Quinvaxem<sup>®</sup>** fully liquid vaccine against five important childhood diseases. **Hepavax-Gene<sup>®</sup>** recombinant hepatitis B vaccine. **Epaxal<sup>®</sup> Junior** low dosage unique aluminum-free hepatitis A vaccine. **MoRu-Viraten<sup>®</sup>** vaccine for protection against measles and rubella. **Epaxal<sup>®</sup>** aluminum-free hepatitis A vaccine. **Vivotif<sup>®</sup>** oral typhoid vaccine. **Dukoral<sup>®</sup>** the only internationally licensed oral vaccine against cholera (and ETEC). **Inflexal<sup>®</sup> V** virosomal adjuvanted influenza vaccine.

## Products continued

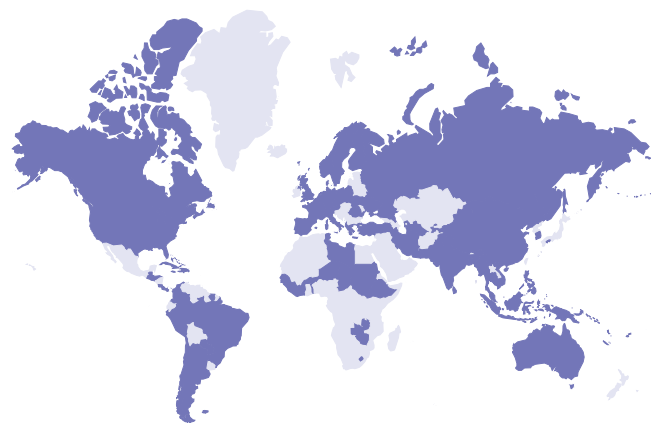
Vaccines play a pivotal role in protecting against diseases and contribute significantly to an improvement in global health.

### Products

Our marketed vaccines currently combat 12 major infectious diseases. In 2009 we distributed more than 115 million vaccine doses in over 100 countries throughout the world. Our product portfolio consists of three distinct focus areas:

- Paediatric
- Travel & endemic
- Respiratory

### Distribution of Crucell products



Crucell products distributed

Untapped markets

### Quinvaxem®

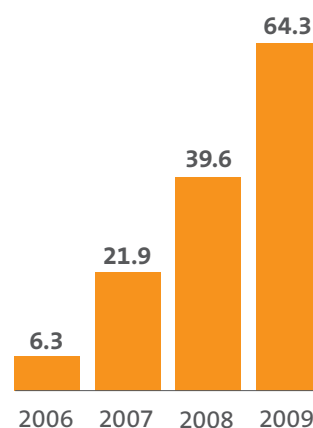


Quinvaxem® is the only fully liquid pentavalent DTwP-HepB-Hib vaccine that is free from the preservative thiomersal. It is an ideal solution for infants and protects against five

potentially deadly childhood diseases: diphtheria, tetanus, pertussis, Haemophilus influenzae type b disease and hepatitis B. In its fifth year in the Extended Programme for Immunization (EPI), over 130 million doses of Quinvaxem® have been delivered to more than 50 countries. In August 2009, supranational organizations renewed a long-term arrangement with Crucell for the supply of \$300 million worth of Quinvaxem® for the period 2010-2012. This figure is projected to grow further over the three year period. Today Quinvaxem® has a market share of over 50%.

#### Quinvaxem® vaccines sold

(Doses in million units)



### Hepavax-Gene®



Hepavax-Gene® is a prophylactic recombinant vaccine against hepatitis B virus infection, providing long-term protection. With a track record of more than 500 million doses

administered worldwide, it is also one of the established WHO pre-qualified vaccines.

### MoRu-Viraten®



MoRu-Viraten® is a safe, well-tolerated and effective vaccine for protection against measles and rubella in children, adolescents and adults. MoRu-Viraten® is free of egg proteins and antibiotics, posing no risk to children with allergies to these substances. The vaccine has been marketed since 1986 and is on the WHO list of vaccines for purchase by UN agencies.

### Epaxal® and Epaxal® Junior



Epaxal® is the only aluminum-free hepatitis A vaccine on the market. The absence of aluminum reduces the pain when injected, making it particularly well-suited to the paediatric market. Epaxal® induces protective antibody levels within 10 days of primary vaccination and provides seroprotection for at least 20 years following the second (booster) dose. Its excellent efficacy and safety have been documented in many clinical trials and it can be fitted into the regular immunization schedule for babies. Epaxal® is licensed in more than 40 countries worldwide. Epaxal® Junior is a low dosage vaccine for the paediatric market with superior tolerability.

### Vivotif®



Vivotif® is a live attenuated oral vaccine for the prevention of typhoid fever. It is the only oral vaccine indicated for use against *Salmonella typhi*, the most prevalent of the enteric fever-causing bacteria. Protective efficacy has been proven in several large-scale field trials and it has an excellent track record for safety, having been on the market for more than 20 years. It is currently licensed in over 30 countries, including the USA. Results suggest that Vivotif® may be unique in also protecting against *S. paratyphi*, another common cause of enteric fever.

### Dukoral®



Dukoral® is a liquid oral vaccine which stimulates the immune response in the intestine to provide 85% protection against diarrhea caused by cholera. It has also shown documented protection against traveler's diarrhea caused by e-coli. Dukoral® was first licensed in 1992 and is now licensed in over 60 countries. It is presently the only internationally licensed oral cholera vaccine. To date, more than 10 million doses of Dukoral® have been supplied and it enjoys an excellent safety record.

### Inflexal® V



Inflexal® V is a virosomal adjuvanted vaccine against influenza, based upon the virosome technology developed and patented by Crucell. It is the only adjuvanted flu vaccine licensed for all age groups (from six months). The vaccine's antigen composition follows yearly WHO recommendations. Inflexal® V was originally introduced in 1997, is registered in 43 countries and has extensive market experience, with more than 49 million doses confirming its safety profile. The tolerability of Inflexal® V is excellent due to its biocompatibility and purity.

We also distribute a variety of other products, such as Gardasil® (Merck) and Prolastin® (Talecris).

## Expanding the scope of our ambitions



As part of Crucell's corporate strategy, The Crucell Ambition, we are working hard to translate our commitment to corporate social responsibility (CSR) into action. In our efforts to further improve global health worldwide, developing our CSR performance and reporting are key priorities for Crucell in the coming years. In the following pages we highlight our standards for doing business in a responsible way.





# Expanding the scope of our ambitions continued

## A pivotal year

Crucell has made important progress in developing its approach to corporate social responsibility (CSR). In 2009 we made the transition from the ambition to focus more on CSR performance and transparency, to a strategy for how to do this. We also created the basic framework necessary for embedding a CSR program in the organization.

A global CSR policy, focusing on the four themes of Performance, People, Planet and Philanthropy, has been outlined. Key performance indicators, ambitions and targets have been defined for each category, and construction of a centralized data management infrastructure is underway. Top-level ownership of the CSR program will support the continuous development of this approach in the years ahead.

This chapter describes where Crucell now stands in terms of CSR performance, where we are heading and how we plan to get there.

The information in this chapter covers the entire organization for the year 2009 unless otherwise stated. Crucell has not sought external verification of the information in this chapter as our current priority is to complete implementation of our systems for CSR information management and reporting.

## CSR highlights in 2009

- Crucell made great progress towards a global, evidence-based system for systematic CSR development and reporting.
- Crucell formulated concrete ambitions and targets in the CSR categories of performance, people, planet and philanthropy.
- Crucell was listed on the Dow Jones Sustainability Index (September 2009).
- Ronald Brus was named biotech CEO of the year at the international Vaccine Industry Excellence Awards.
- Crucell and Johnson & Johnson signed a landmark agreement based on Crucell’s unique capabilities for healthcare innovation; the billion-euro deal provides an enormous boost for these capabilities.
- Crucell started introducing the FlexFactory®, a revolutionary approach to manufacturing. Substantial reductions in pipeline development times and production costs (for new products) are expected.
- Crucell professionalized its procurement organization, thereby laying the foundation for responsible supply chain management.
- Crucell launched ‘Footprint’, its own outreach program. The program will bring Crucell employees and people in disadvantaged communities together, in ways that benefit both groups.

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## Crucell's responsibility to society

### Doing business with a warm heart and a cool head

Crucell is deeply committed to being a good corporate citizen: a company that creates significant value for society. Our mission is to make a truly meaningful contribution to global health by directing our proven talent for innovation towards the fight against infectious diseases. An entrepreneurial mind-set and social responsibility go hand-in-hand at Crucell.

We focus on major health threats that demand innovative solutions, striving to lead rather than to follow. Wherever we can, we focus on disease prevention rather than cure, knowing that this approach offers the best protection for societies' economies as well as for the individuals in these societies. We focus, too, on business growth and operational excellence, so that we can deliver sustainable benefits to all our stakeholders—from the people who use our healthcare products to those who invest in our company.

By running Crucell 'with a warm heart and a cool head', we aim to generate sustainable profit, measured in both healthcare and financial terms. Revenues from product sales, technology licensing and partnerships are reinvested in our innovation and discovery programs, the acceleration of new product development in our research & development (R&D) pipeline, and activities to expand access to our marketed products. Savings derived from greater operational efficiency are also used to further Crucell's core business of healthcare innovation. Fuelling this virtuous cycle of business and health benefits is Crucell's primary corporate social responsibility.

### Health and wealth

The essential link between health and wealth is well established. An extensive body of evidence indicates that healthier individuals and societies are better off financially, and that effective primary healthcare—especially disease prevention—is crucial for socioeconomic development. These insights are fundamental to the United Nations' Millennium Development Goals.

### An increasingly urgent mission

Crucell's commitment to innovation and focus on infectious diseases is becoming all the more important in the face of worldwide trends affecting health and well-being.

- Globalization and urbanization are promoting infectious diseases spread by insects or water, such as dengue fever, cholera and typhoid fever. Respiratory diseases like tuberculosis (TB) especially affect the urban poor.
- Climate change and weather extremes are changing the incidence or geographical distribution of vector-borne diseases like malaria and dengue fever.
- Mobility and ease of travel are increasing the rapid global spread of infectious diseases like tuberculosis and influenza, as well as increasing the risk of ruined holidays for travelers to exotic locations.
- Population growth and aging are associated with a growing prevalence of infections carried in food and water that cause intestinal diseases like cholera, typhoid fever and hepatitis A.

**“By running Crucell ‘with a warm heart and a cool head’, we aim to generate sustainable profit, measured in both healthcare and financial terms.”**

## Expanding the scope of our ambitions continued

**“We work to bring significant benefit to the lives of people worldwide by recognizing our wider responsibility to society.”**

### Wider responsibilities

We are committed to conducting our business with integrity, in a way that respects the rights and needs of our large network of stakeholders, inside and outside the company. We value—and invest in—being a company that talented people want to work with and for.

We want to help protect our planet by minimizing our environmental footprint and making sustainable practices a priority in our company. At present, Crucell is the smallest of the major vaccine companies—though growing very fast—and therefore our manufacturing operations are relatively modest. However, we are committed to identifying and seizing opportunities to improve performance in this area. This also means working proactively in anticipation of future growth.

We also place great value on doing more to benefit society than we strictly ‘must’ do in accordance with Crucell’s mission: bringing innovation to global health. This commitment embraces everything from the sharing of scientific knowledge to community outreach programs.

### Our stakeholders

Crucell works to bring significant benefit to the lives of people worldwide. This requires constructive interaction with a large number of stakeholders, including employees, legislators, investors, policy makers, business partners, licensees, suppliers, customers and organizations dedicated to sustainability issues.

Our external stakeholders are far too numerous to mention, but in the interests of transparency here is a shortlist of key examples.

- Legislators: US Food and Drug Administration, European Medicines Agency, and national regulatory authorities.
- Investors: the Dutch association of investors for sustainable development, Johnson & Johnson, Aviva.
- Policy makers: World Health Organization (WHO), Pan American Health Organization (PAHO), GAVI Alliance.
- Business partners: Johnson & Johnson, DSM Biologics, Merck, Novartis, sanofi pasteur, Wyeth and MedImmune.
- Customers: Supranational purchasing organizations such as Unicef (on behalf of developing countries); public and/or private health organizations in developed countries.
- Sustainability organizations: Dow Jones Sustainability Index, Carbon Disclosure Project.

### Stakeholder engagement

We choose our business partners carefully, seeking above all a shared commitment to business integrity and healthcare innovation. We require our suppliers to comply with the Crucell Code of Conduct, our commitment to adhere to the highest ethical and legal standards in all aspects of our business.



Our ambition is to make sustainability issues an integral part of our ongoing dialogue with stakeholders. During 2009 we laid the basis for realizing this, for example by establishing a global procurement policy that will enable continuous improvement in responsible supply chain management.

As part of the rebranding process leading to the launch of the global Crucell identity in November 2009, Crucell asked a diverse group of stakeholders (approximately 30; half internal and half external) for feedback on how they perceive Crucell in relation to CSR issues. The external participants included representatives of a non-governmental organization, a distributor, business partners, travel clinics, the nursing profession, an employment agency and a financial analyst, among others.

The survey results showed that stakeholders generally perceive Crucell as a responsible corporate citizen. All found CSR to be an important issue for Crucell, particularly in view of its core business. They felt that Crucell should do more to raise awareness of its CSR activities and to communicate these activities. This advice has helped to shape the development of Crucell's CSR policy and plan. We see this example of stakeholder engagement as a first step towards establishing an active dialogue about CSR issues with our stakeholders worldwide.

## Expanding the scope of our ambitions continued



### Transparency: Developing our approach to CSR

#### **Towards a systematic approach**

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Crucell is a dynamic and creative organization that encourages employees at all levels of the company to show initiative and take responsibility. We see that many innovations relating to corporate social responsibility (CSR), among other fields, happen because of the passion, inspiration and insights of individuals closest to a work process. During 2009 there were many examples of that Crucell spirit in action.

We recognize that Crucell can contribute even more to society by formulating shared CSR goals and addressing these in a structured way. In 2008, Crucell took the first steps towards a more comprehensive and transparent approach to CSR.

In 2009, significant advances have been achieved where we made the transition from a working ambition to make Crucell's CSR more prominent in the organization and more transparent for the outside world, to a strategy for how to do this. We also started building the glide path from where we are, to where we want to be. We have moved forward, step by step, using an approach that fits our corporate culture and our stage of development.

#### **Building the system**

---

Initially, current practices relating to CSR were surveyed by interviewing a large number of employees from a broad cross-section of functions and sites. This survey revealed a strong interest in CSR and a wide range of initiatives making a tangible contribution to the development of CSR awareness and good practices. Examples are described later in this chapter. The survey also highlighted the need for a more systematic and consistent approach to CSR, guided by a

global policy and clear targets, and supported by appropriate tools for measuring and reporting CSR performance against these targets.

Armed with this information, Crucell created the framework necessary for embedding a mature CSR program in the organization. This framework includes the outlines of a global CSR policy, key performance indicators, construction of a centralized system for managing information relevant to CSR (see footnote page 43), a working group and meeting structure, and a system of governance. Overall ownership of CSR has been taken on by Chief Executive Officer Ronald Brus, ensuring top-level support for its ongoing development. Chief Operating Officer Cees de Jong is responsible for operational aspects. Crucell's CSR program and progress will be discussed at Management Board meetings and in formal meetings of the CSR working group at least two times a year.

Concrete CSR ambitions and targets for the coming years were defined by Crucell's Management Board after reviewing the outcomes of the interviews with employees throughout the organization. This approach is consistent with Crucell's culture, which values open dialogue in the process of decision making. It also establishes a springboard for the rapid implementation of CSR policy and adherence to the targets set.

Details of Crucell's CSR system, including responsibilities, key performance indicators and targets are given in the final section of this CSR chapter.



## CSR benchmarks



Crucell's baseline performance on external benchmarks of CSR reporting is good.

Crucell was listed on the Dow Jones Sustainability Index (DJSI) on September 3, 2009, in recognition of the significant steps the company has taken to define and develop its commitment to sustainability issues. We are very proud of this achievement. The DJSI was introduced in 1999 to indicate international corporations that have made sustainability an integral part of their business strategy. Companies are included on the basis of best-in-class performance.

Another objective measure of Crucell's progress in CSR development is Crucell's participation in the Carbon Disclosure Project (CDP) in 2009. This project is a worldwide, investor-driven initiative encouraging multinational corporations to report on their environmental impact, specifically in relation to carbon emissions and climate change.

In the Netherlands, where Crucell has its global headquarters, the Company's performance in CSR reporting showed good progress in 2009 compared to the previous year. Crucell's overall score rose 17 points on the 100-point 'Transparency Benchmark', an index published by the Dutch Ministry of Economic Affairs. This placed Crucell in the top three companies showing fastest progress.



Crucell's next challenge regarding CSR reporting will be to meet the comprehensive criteria established by the Global Reporting Initiative (GRI). This international standard of

CSR transparency demands much more data, and more performance measures, than we had access to in 2009. The systematic approach introduced in 2009 lays the foundation for achieving our ambition to continuously improve our level of GRI compliance and reach A level in 2015. Details of our current GRI compliance (self-declared C level) can be found on our website: [www.crucell.com/commitment\\_to\\_csr](http://www.crucell.com/commitment_to_csr).



## Expanding the scope of our ambitions continued



“Taking the next leap forward in CSR is an important focus for us.”

Recording, measuring and reporting on our CSR performance in a verifiable and comprehensive way demands considerable ongoing investment of time, effort and money. Crucell's Management Board considers this a priority for several reasons. First, we see transparent communication about CSR to be a social responsibility in itself. Second, we believe that by achieving greater insight into our impact on society, we will be best able to weigh up the multiple considerations that shape our strategic decision making. We want a CSR system that will enhance the virtuous cycle of innovation that links business profit with health and its associated socioeconomic benefits.

### A supportive environment for CSR

The growing maturity of Crucell's approach to CSR has to be seen in the context of Crucell's overall organizational development.

In 2009, Crucell implemented a wide range of programs designed to facilitate the integration of the Company's historically separate components, streamline processes and capture synergies, improve data management and promote cost-efficiency. Many of these initiatives emerged from the operational excellence program launched at the start of 2008. All are directed towards a single strategic goal: creating a sustainable business model that lives up to Crucell's ambitious promise to bring innovation to global health.

The launch of the global Crucell brand on November 16, 2009, expresses the new maturity of our organization and our growing impact on world health. Crucell embarked on an ambitious mission in 2006 by acquiring Swiss vaccine maker Berna Biotech, SBL Vaccines of Sweden, and Berna Products Corporation. With these acquisitions, Crucell became the largest independent vaccine company in the world. Three years later, global branding is a logical and necessary step to display the innovative power of today's Crucell—an integrated, global organization. Even more importantly, it will help to strengthen our business and the contribution we can make.



## “Global branding fits our ambition to increase transparency and visibility.”

Global branding fits Crucell's ambition to increase transparency and visibility. It supports a more harmonized way of working within the company and towards external stakeholders.

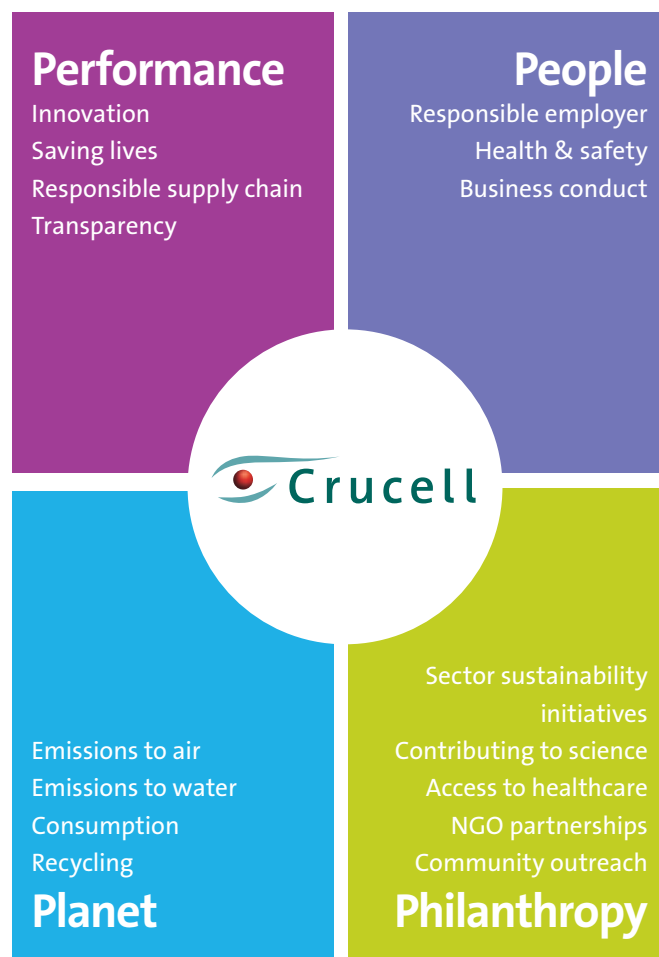
Crucell's transition towards a more centralized, systematic and transparent approach to CSR is supported by this evolution. Indeed, without the global policies and practices established in 2009, taking this next leap forward in CSR would not have been possible.

### A global CSR policy

Crucell's global CSR policy is founded on a four-part framework (see 4P Framework on the right), corresponding to the four main ways in which we want to make a positive contribution to society. This organizational principle is to some extent artificial. In practice, there is considerable overlap among the four categories, pointing to the interdependence of CSR activities. Crucell's policy provides the overarching vision needed to coordinate these efforts.

In the next section of this CSR chapter, we discuss Crucell's activities in each of these four categories during 2009.

### A '4P Framework' as a foundation for a CSR Policy



This framework system (Reporting Manual), now under construction, includes definitions of performance indicators, instructions for CSR reporting (how, what and who) and an information management tool. The Reporting Manual is being custom-built to fit Crucell's organization and CSR policy. Roll-out of the Reporting Manual company-wide in 2010 is one of the quantitative targets set by Crucell's Management Board.

## Expanding the scope of our ambitions continued

### Review: Crucell's contribution to society in 2009

#### Performance

Under the umbrella of 'Performance' are grouped the four aspects of CSR that relate most directly to Crucell's core business: innovation, saving lives, responsible supply chain and transparency.

By the latter, we mean the responsibility to evaluate and report on our CSR activities in a comprehensive and systematic way. As discussed in section two of this chapter (Transparency: Developing our approach to CSR), we have made significant progress towards greater CSR transparency by outlining a global policy and initiating an evidence-based CSR system. The key performance indicators, ambitions and targets defined are covered in detail in section four: 'The way forward: Crucell's CSR ambitions, targets and tools'.

#### Creating value through innovation

Innovation is the foundation on which Crucell was built, and the fuel driving us forward. It is the key to achieving the virtuous cycle of sustainable business and health gains that lies at the heart of our strategic and CSR ambitions. 2009 was a breakthrough year in this regard.

The revolutionary influenza antibody research going on in our innovation & discovery (I&D) group, led by Chief Scientific Officer Jaap Goudsmit, attracted the world's largest healthcare company, Johnson & Johnson (JNJ), to sign a truly extraordinary agreement with Crucell in September, 2009. Crucell's scientists have discovered antibodies that cross-neutralize influenza viruses of different subtypes (including H5 and H1) and provide immediate protection against a broad range of flu strains in pre-clinical models.

The agreement with JNJ guarantees full funding for bringing our flu antibodies to market as quickly as possible and expanding our I&D programs. A payment of more than €300 million for JNJ's minority stake in Crucell also provides an immediate cash injection for our other pipeline programs, which are developing much-needed solutions for malaria, tuberculosis, rabies and other major threats to human health.

The partnership with JNJ is the latest in a string of partnerships Crucell has forged over the past few years with leading industry and academic organizations. For more information on Crucell's agreements with strategic business partners (including DSM Biologics, JNJ, MedImmune, Merck, Novartis, sanofi pasteur and Wyeth) go to [www.crucell.com/partners](http://www.crucell.com/partners). There you will also find a full listing of our numerous research & development partners and licensees.

We choose our business and scientific partners carefully, seeking above all a shared commitment to healthcare innovation and integrity. We invest significant time and energy into building and maintaining good relationships with these partners. Open communication and regular evaluations are an essential part of this.



### The FlexFactory®: a paradigm leap offering exciting benefits

The FlexFactory® can most simply be described as a modular system of mobile clean rooms containing lightweight, mobile equipment based on disposable technology—that is, all parts of the equipment that come into direct contact with the biological material are disposable.

In contrast to a traditional manufacturing facility, with its cumbersome stainless steel bioreactors and separate, airlocked clean rooms for the various manufacturing steps, the FlexFactory® is extremely compact, flexible and mobile. It is also highly cost- and energy-efficient, as the use of disposables eliminates the need for complicated cleaning and sterilization of equipment between production batches.

What makes this 'lean and green' innovation truly revolutionary, however, is that it transforms the approach to product development—in ways that reduce the risks inherent in biopharmaceutical innovation and the time required to bring a new product to market.

At present, biopharmaceutical manufacturers invest in equipment and a facility specifically designed for the manufacture of a new product long before that product reaches Phase III (the last phase of testing in humans, and the final hurdle before regulatory approval for commercialization of a new product). This is necessary because the regulatory authorities require that Phase III clinical trial material is manufactured in the same set-up—using the same process—that will be used for manufacturing the commercial product.

The FlexFactory® breaks this traditional paradigm. Because of its mobility and flexibility, the FlexFactory® can be recreated in any location. "Once you have a positive outcome with a candidate product in Phase III, you go to the final manufacturing site and install the



This image is the property of Xcellerex, Inc.

**"This 'lean and green' innovation reduces the risks inherent in biopharmaceutical innovation."**

same equipment used for Phase III manufacturing," explains Alain Pralong, Crucell's Senior Director Process Development. "As well as saving a lot of time, this continuity will allow us to develop a process that fits our manufacturing platform—the FlexFactory®—rather than building expensive facilities to fit a process."

It is estimated that full implementation of the FlexFactory® will substantially reduce capital expenditure, cut operating costs and possibly shrink the average development time for a new, best-in-class compound to as little as eight years, compared to the current 11–15 years.

## Expanding the scope of our ambitions continued

In 2009, Crucell took an exciting, proactive step in anticipation of future development by starting to introduce a revolutionary approach to manufacturing called the FlexFactory®. This is a pioneering move: when the FlexFactory® is fully implemented, Crucell will be the first in the world to have a biotech manufacturing process that is conducted from start to finish using only disposable equipment. This approach will significantly reduce development timelines for our pipeline products and slash energy consumption during manufacturing, compared to traditional facilities (see box about The FlexFactory® on previous page).

“The disposables strategy brings down operational costs so significantly that it enables us to consider making therapies for indications that we could not have considered before,” says Chief Executive Officer Ronald Brus. “And it is a perfect fit with our high-yield, cost-efficient PER.C6® human cell line technology, which was designed to make affordable and innovative new therapies possible.”

In recognition of the visionary leadership that has made Crucell the world's largest independent vaccine maker, Ronald Brus was named Biotech CEO of the Year at the Vaccine Industry Excellence Awards, held in Washington in April, 2009.

# PER.C6®

Designed to make  
affordable and innovative  
new therapies possible.

### Preventing illness and death

In 2009, Crucell distributed more than 115 million vaccine doses in more than 100 countries around the world, with the vast majority of doses (94.7%) going to developing countries, where the burden and impact of infectious diseases are greatest. Crucell's current portfolio of marketed vaccines provides protection against a total of 12 major diseases. Based on the best available evidence regarding vaccine efficacy, disease incidence and case fatality, in 2009 Crucell's 'top five' vaccines\* prevented 3.6 million cases of infectious disease and 819,000 deaths that would have been caused by these diseases in unvaccinated populations. This calculation assumes a vaccine waste rate of 2%.

Comparison with previous-year figures demonstrates that Crucell has strengthened its impact on global health in 2009 by expanding vaccine sales and markets. In 2008, we reported more than 100 million vaccine doses had been distributed for the protection of people in more than 80 countries. This translated into the prevention of an estimated 3.1 million cases of infectious diseases and over 700,000 deaths among these cases in 2008.

### Quinvaxem® and beyond

Sales of Crucell's lead product Quinvaxem® showed strong growth in 2009, continuing the trend seen since the launch of this innovative pentavalent (five-in-one) vaccine towards the end of 2006 (see page 32 for details). Quinvaxem® combines the vaccines against five deadly childhood diseases into a single injection. Developed specifically to meet the needs of the world's poorest communities, Quinvaxem® is making an important contribution towards achieving the United Nations Millennium Development Goals, in particular the target of reducing the under-five mortality rate by two-thirds between 1990 and 2015.

\*Crucell's top five vaccines in terms of sales are Quinvaxem®, Hepavax-Gene®, Epaxal®, Inflexal® V and Vivotif®.



“In 2009, Crucell distributed more than 115 million vaccine doses in more than 100 countries. Crucell’s ‘top five’ vaccines prevented 3.6 million cases of infectious disease and 819,000 deaths.”

The initial success of Quinvaxem® owed much to its innovative formulation and presentation. It was the first fully liquid vaccine of its kind, ready for use without further preparation by healthcare workers in the field, and its presentation in single-use vials reduces the risks of vaccine contamination or waste. These are key considerations for communities struggling to cope with hygiene problems and to make the best use of limited healthcare resources. Now that other manufacturers are starting to bring similar vaccines to market, Crucell’s outstanding track record for quality, productivity and reliability—all along the supply chain—is becoming increasingly important for maintaining our competitive advantage. The new awards for supply of Quinvaxem® placed by supranational organizations in 2009,\* confirm Crucell’s added value in this regard.

Throughout 2009, Crucell’s Korean organization achieved remarkable results in upscaling the production of Quinvaxem® and Hepavax-Gene® while simultaneously making rapid progress on the construction of a new manufacturing facility in the Incheon Free Economic Zone. The new plant will enable further increases in production capacity and efficiency in order to meet anticipated growing demand for Crucell’s pentavalent and hepatitis B vaccines.

Meanwhile, Crucell continued to work on life-cycle development of our existing products in order to maximize the creation of value—measured in human and commercial terms. Examples are our efforts to launch Epaxal®, Crucell’s hepatitis A vaccine, on the US market and to widen the indications (registered medical uses) of our vaccine Dukoral® in those countries where it is only registered for the prevention of cholera. Dukoral® also has proven efficacy for preventing traveler’s diarrhea caused by ETEC, an *E. coli* bacterium common in resource-limited regions. We made important progress in both areas during 2009.

\*Since the launch of Quinvaxem® in October 2006, Crucell has received awards of US\$0.8 billion for the supply of Quinvaxem®; US\$0.5 billion for the tender period 2007-2009 and a further US\$0.3 billion in the first round of awards for the 2010-2012 tender period. The supranational organizations have so far awarded approximately half of the volume for this tender period.

## Expanding the scope of our ambitions continued



# €30 mln

“The Healthy Ambition program delivered over €30 million in run-rate savings.”

### Creating value through operational excellence

Crucell's operational excellence program, Healthy Ambition, headed by Cees de Jong, Chief Operating Officer, was successfully completed in 2009, delivering valuable efficiency improvements and the targeted run-rate savings of over 30 million Euros. All the money saved is being reinvested into building the business, with a key focus on investments in research & development (R&D). This is in line with our strategy to use strong operating cash flow to accelerate new product development.

However, this is only the beginning of Crucell's efforts to create value through operational excellence. Through Healthy Ambition we have set in motion a program that is expected to gather momentum for the years to come, as initiatives emerging from the program are fully implemented and trigger further improvements.

One of many examples is the restructuring of Crucell's global business into three franchises (paediatric, travel & endemic, and respiratory), each with its own Business Manager. This structure provides overview, facilitates planning and enables processes to be managed more efficiently, with even closer cooperation between our scientists and our business people.

As an organization, we made a big leap forward in development and implementation of global policies and global systems in 2009. These are essential tools for achieving further, sustainable improvements in operational efficiency, information management, transparency and strategic decision making. They lay the basis for embedding sustainability in our organization.





### Building a responsible supply chain

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Crucell sees the continuous improvement of its own operational processes as a key aspect of responsible supply chain management. We also recognize that optimal management of our supply chain, from a CSR perspective, goes beyond this focus on operational excellence. Our ambition is to continue developing in this area, so that issues relating to CSR can be systematically incorporated into our choice of suppliers and our relationships with them in 2011.

Important progress towards this goal was achieved in 2009 through the professionalization of Crucell's procure-to-pay (P2P) organization. First, an in-depth analysis of Crucell's global spending patterns was conducted, using an automated tool for data collection and analysis. This provided an overview of all Crucell's suppliers, together with the costs, volumes and categories of goods and services purchased worldwide. It also highlighted opportunities for improvements, over and above those achieved in the first phase of our operational excellence program.

These insights formed the basis for a strategy aimed at achieving sustainable excellence in the way we purchase equipment, supplies and services. A key focus was to leverage our power as a global organization by introducing common procurement practices throughout the company, rationalizing suppliers, bundling order volumes, aligning terms and conditions, and so on.

Crucell moved swiftly to implement these improvements, starting with a global procurement policy incorporating best practices. This has been communicated to all employees worldwide. A tool for monitoring P2P performance and promoting employees' adherence to global policies has been introduced. This system of ongoing data collection and category-based analysis, at the global level, is an essential prerequisite for greening the supply chain.

We have also drawn up new general terms and conditions for vendors, which specifically refer them to Crucell's Code of Conduct and require that they comply with this code in their dealings with Crucell. This is a first step in the continuous improvement of responsible supply chain management from a CSR perspective.

At our site in the Netherlands, a tangible benefit of smarter procurement practices has been the reduction of chemical waste. By centralizing the purchase and management of chemicals used in the Leiden laboratories, the facilities group has significantly cut the amount of chemicals that are purchased and can make sure that supplies are used before their expiry dates. The environmental, safety and efficiency gains are obvious.

## Expanding the scope of our ambitions continued



### Dealing with CSR dilemmas

Corporate social responsibility lies at the heart of Crucell's mission to bring innovation to global health and make a meaningful difference to the lives of people worldwide. In general, what is good for Crucell's business is good for society. Nevertheless, we are sometimes confronted with difficult choices between opposing responsibilities.

What to do, for example, if we see the opportunity to develop a life-saving product that does not look attractive from a purely commercial point of view? Crucell was faced with that dilemma several years ago, when our scientists discovered a mix of monoclonal antibodies (mAbs) with the ability to neutralize the rabies virus. "Initially, the market for this rabies product appeared to be small and unprofitable," recalls CEO Ronald Brus. "But with 55,000 people dying in terrible suffering from rabies each year, and solid evidence that our rabies antibodies could prevent these deaths, we decided to proceed with development, in partnership with sanofi pasteur."

It soon became apparent that in taking this humane course, Crucell also made a sound business decision: the potential commercial value of this innovative rabies product is significant. Using Crucell's highly cost-effective production method based on PER.C6®

technology, the rabies mAbs can be produced at much lower cost than the blood-derived antibody product now on the market. The cost reduction is so substantial that many countries that cannot afford the currently available antibody treatment will be able to buy the mAb product. This will open up new markets, making our rabies program a profitable venture as well as a humanitarian one.

The example of rabies illustrates the ideal resolution of a dilemma: achieving the optimal balance between different responsibilities. More often, one responsibility must take priority over another. For example, it is not always possible to give equal attention to operational and environmental concerns.

The construction of Crucell's new manufacturing facility in Incheon, Korea, illustrates this sort of dilemma. We have a responsibility to get this new production plant for Quinvaxem® and Hepavax-Gene® up and running as soon as possible, in order to meet the growing demand for these vaccines and ensure continuity of supply. Crucell therefore made the decision to design the new plant along the lines of the old one—while incorporating efficiency and capacity improvements—rather than starting from scratch to design a 'green' facility. This approach has enabled very fast progress on the construction of the new plant and should facilitate its approval by the regulatory authorities. At the same time, Crucell is moving towards 'lean and green' manufacturing of its future products by introducing the FlexFactory® (see page 45), a revolutionary approach to biopharmaceutical production.

Packaging is another area where we have to weigh up conflicting interests. See page 57 for an example.

Our Swedish organization has launched a very successful program for recycling cool boxes—the temperature-controlled containers that keep vaccines in good condition during transport. Normally, customers throw the boxes away once they have unpacked the vaccines. Crucell employees in Sweden came up with the idea of asking their customers in the Nordic region to return the boxes for reuse. Crucell pays for the return transport, which amounts to approximately half the cost of purchasing the cool box, and reuses each box up to four times before disposing of it in an environmentally responsible way. When the project started in September 2009, the target return rate was 60%. The response has far exceeded expectations, reaching 94% within three months. Crucell is now looking into the feasibility of widening the program to include other regions.

Since the start of 2009, 100% of the electricity consumed at our Dutch site has been 'green' energy, generated by sustainable sources. This is a good example of how our local managers are already working on responsible sourcing. With the roll-out of the global CSR policy and reporting manual in 2010 we aim to build on this foundation.

**Animal welfare.** Before any candidate medical product can be given to humans, it must be rigorously tested in pre-clinical (non-human) models. Crucell performs animal testing to the minimum extent that is required by law. We conduct essential safety studies in animals in accordance with the highest international standards, which are designed to prevent or minimize any suffering of the animals tested. Simultaneously, we apply the 3R principles—Reduce, Refine and (ultimately) Replace—to pre-clinical studies involving animals. Crucell has been working over many years to replace animal tests with cell-based assays, and these efforts have already resulted in the significant reduction of animal testing.



“What is good for Crucell’s  
business is good for society.”

# 100%

Since the start of 2009, 100%  
of the electricity consumed  
at our site in the Netherlands  
has been 'green' energy.

## Expanding the scope of our ambitions continued

### People

The category 'People' encompasses Crucell's responsibilities regarding employees, health and safety, and business conduct.

#### Being a responsible employer

Crucell's ability to make a difference to world health depends on the creativity, passion and drive of the employees making up our global organization. We are working hard to attract people with these qualities and to create the sort of environment that will inspire, empower and challenge them.

Crucell is growing fast—in 2009 our global workforce expanded by 11% compared to 2008—in line with our business and healthcare ambitions. The majority of the recruitment was in Leiden, the Netherlands, where we are building our research and development capabilities, and in the United Kingdom, where we launched our own marketing & sales organization in October. The experienced UK team will enhance the visibility and strengthen sales of Crucell's travel vaccines in this high-potential market.

Staff turnover has decreased markedly, from 18.44% in 2008 to 13.12% in 2009, suggesting that our focused efforts in relation to people and organization development are bearing fruit. (Note that the human resources statistics reported in this section are based on the available data from Crucell's five main locations, employing over 90% of the total workforce. With the implementation of the Reporting Manual we aim to achieve full coverage in 2010).

**“We are working hard to make Crucell an employer of choice.”**

In 2009 we completed the leadership development program initiated in 2008: managers at all levels have now participated in this program, which emphasizes self-insight as the starting point for good leadership. All managers receive full-circle feedback (from direct reports, peers, and their own managers) as an integral part of annual performance assessments. We intend to extend this approach to include all employees. The percentage of employees receiving regular performance reviews increased to 95% in 2009, and we are aiming for full coverage in 2010.

Senior managers took part in a program to emphasize their responsibility as role models in the organization. We believe that adherence to the Crucell Values—Integrity, Respect, Complementarity, Reliability, Innovation, Passion and Drive—has to be led by example from the top. These values were also reinforced company-wide in 2009 through numerous activities initiated by our Corporate Communications and Human Resources departments. For example, all employees received a birthday calendar highlighting the values.



Our employees' opinions matter to us. As in 2008, last year monthly questionnaires were sent to 100 randomly selected employees, asking them for their views on a wide range of issues relating to The Crucell Ambition, Crucell's corporate strategy for developing the business. The surveys invite employees to comment on the progress being made and further improvements needed in the organization. In addition, informal lunch meetings between Crucell's CEO Ronald Brus and small groups of employees were held on a regular basis, with the aim of sharing perspectives among a broad cross-section of our people.

During 2009, we placed strong emphasis on raising CSR awareness and participation among our employees. You can read more about these activities in the section on 'Philanthropy' (see page 71).

Crucell sees the value of diversity and strives to foster this, both in its recruitment practices and organizational development. Our Dutch and Swiss sites each employ people from 20 different nationalities, and our approach to operational excellence is based on teamwork across sites and functions. This cultural and functional mix generates new insights for improving our business processes and is vital for building a unified, fully integrated global company.

We are seeing a growing sense of belonging and common purpose among our employees around the world, largely thanks to this approach. The energetic efforts of our Corporate Communications team, supported by local members of our Global Communications Network, also play a vital role.

The number of female employees in our workforce increased by 16% in 2009 compared to the previous year, bringing the percentage of women in the organization to 45% (up from 43% in 2008). The relatively low number of women in senior management positions is a point for attention. However, Crucell is committed to recruiting and promoting employees on the basis of talent and ability, without negative or positive discrimination on the basis of gender, race or age.

In 2010 our global human resources team will implement an ambitious learning and development program for all Crucell employees. The aim is to facilitate and encourage our people at all levels of the organization to continuously develop their skills and knowledge. By supporting our people's opportunities to learn and grow, we aim to become a stronger company that attracts and retains the right people. Our ambition is to become an 'employer of choice'.

### Health and safety

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Protecting the health and safety of our employees is a moral obligation and essential for achieving our business goals.

Improving safety awareness was firmly on Crucell's agenda in 2009. In line with objectives, safety training was improved at all Crucell sites and all local safety officers were sent to DuPont safety training, the gold standard in the chemicals and biopharmaceutical industry.



## Expanding the scope of our ambitions continued

**Table 1**

We value both gender and ethnic diversity and accordingly act as an equal opportunity employer.

The characteristics of our workforce are as follows:

	China	Italy	Korea	Netherlands	Spain	Sweden	Switzerland	UK	USA	Total
<b>2009</b>										
Number of male employees	9	10	169	181	33	43	218	6	12	681
Number of female employees	41	8	50	177	40	78	151	15	7	567
<b>Total number of employees</b>	<b>50</b>	<b>18</b>	<b>219</b>	<b>358</b>	<b>73</b>	<b>121</b>	<b>369</b>	<b>21</b>	<b>19</b>	<b>1,248</b>
Average age of employees	30	46	36	36	45	45	40	40	44	40
Number of women in management	1	2	5	27	3	4	14	0	2	58
Number of nationalities per location	1	1	4	20	2	7	20	3	5	n/a
<b>2008</b>										
Number of male employees	9	12	167	139	30	45	225	n/a	11	638
Number of female employees	26	10	44	114	39	88	159	n/a	8	488
<b>Total number of employees</b>	<b>35</b>	<b>22</b>	<b>211</b>	<b>253</b>	<b>69</b>	<b>133</b>	<b>384</b>	<b>n/a*</b>	<b>19</b>	<b>1,126</b>
Average age of employees	31	44	35	36	46	45	42	n/a	43	40
Number of women in management	3	3	4	23	2	10	10	n/a	3	58
Number of nationalities per location	2	1	3	19	2	4	10	n/a	5	n/a
<b>2007</b>										
<b>Total number of employees</b>	<b>30</b>	<b>38</b>	<b>162</b>	<b>325</b>	<b>66</b>	<b>129</b>	<b>357</b>	<b>n/a</b>	<b>19</b>	<b>1,126</b>

\*Not applicable, as Crucell's UK organization was launched in October 2009

	2009	2008
Percentage employee turnover	13.20%	18.44%
Percentage of employees in collective bargaining	17%	20%
Percentage of employees receiving regular performance reviews	95%	93%

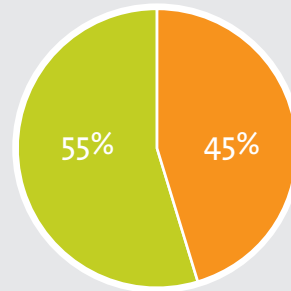
The number of accidents reported to safety officers at our five manufacturing and/or development sites (which employ over 90% of Crucell's total workforce) showed a marked decrease of 21% in 2009 compared to the previous year (27 versus 34 accidents in 2008) despite a significant increase in both our production volume and total number of employees. The majority of these accidents were minor and generic in nature, although a number of potentially serious 'near misses' were reported. It is important to note that Crucell's accident rate is low and that statistical variability has a large impact on the total figures. Therefore, these results must be interpreted with caution. Significant conclusions cannot be drawn from a comparison of only two data points. Having said that, Crucell is committed to accident prevention and is making ongoing efforts at all sites to continuously reduce the number of accidents.

The reliability of safety reporting also improved in 2009, thanks to a more harmonized and centralized approach to data collection. Progress was made in developing a global Environment Health & Safety (EHS) policy in line with international standards and certification schemes. We can also report improvements in terms of raising safety awareness, sharing knowledge, and introducing best practices across the organization.

While these developments are encouraging, we see the need to further improve the way we manage EHS data at the global level. Access to more detailed information, collected from all sites using the same definitions, will give us greater power to improve safety using a 'plan-do-check-act' approach. The introduction of the CSR Reporting Manual, as described earlier in this chapter, will enable this next step in EHS development.

In the face of the emerging influenza pandemic (H1N1) 2009, Crucell took rapid action to protect employees from infection and provide balanced information. Trained nurses in our Swedish organization vaccinated more than 200 employees and family members against the pandemic virus, as part of a government mass vaccination campaign. The government had asked for help with this enormous task, calling on people with healthcare qualifications to volunteer. Similar actions were taken at various other Crucell sites.

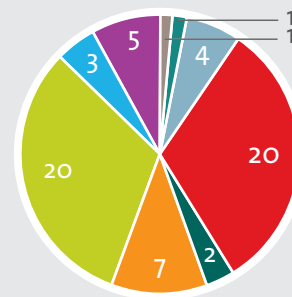
#### Male/female ratio of Crucell employees in 2009



Male

Female

#### Number of nationalities per Crucell facility in 2009



China

Italy

Korea

Netherlands

Spain

Sweden

Switzerland

UK

USA

## Expanding the scope of our ambitions continued



**“Crucell adheres to high standards of ethics and transparency in dealing with all stakeholders.”**

Crucell offers free vaccination against seasonal influenza to employees and their families each year, in countries where this is feasible and appropriate. In the round of vaccinations held in the fall, more than 1770 people worldwide took advantage of this offer. The free shot was given to a total of 245 Crucell employees and their relatives in the Netherlands, 114 in Switzerland, 697 in Korea, 93 in Sweden, 521 in Spain, around 80 in China, and 23 in Italy. Crucell's employees in Argentina were eligible for free immunization under their health insurance scheme. Inflexal® V could not be offered to our people in the United States, as the product is not registered in that country.

### Good business conduct

Crucell adheres to high standards of ethics and transparency in dealing with all stakeholders. We take our legal and ethical obligations very seriously. During 2009 we invested significantly in efforts to ensure compliance with these principles and requirements.

Crucell's Code of Conduct was presented and explained to all employees during interactive meetings led by representatives of senior and local management. The Code of Conduct is Crucell's commitment to business integrity. It guides employees in the high standards of behavior expected of them and their obligation to act with integrity at all times.

The Code of Conduct urges employees to report any behavior or action that may be in breach of this code. In 2009, a procedure for reporting non-compliance was implemented, and compliance officers were appointed worldwide. They report that employees are increasingly seeking informal advice if they are unsure about the ethical way to behave in a particular situation—a positive sign that compliance awareness is increasing.

The Code of Conduct has been incorporated into Crucell's new general terms and conditions for suppliers. This lays the basis for enforcing compliance and responsible supply chain management.

These developments are part of our overall effort to improve enterprise risk management—which includes, but goes beyond, the management of financial risks. In 2009 Crucell invested significantly in the analysis of potential business risks, the establishment of risk management procedures, and the training of relevant employees in policies and procedures, for example anti-corruption strategies.

## Planet

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Crucell is conscious of its responsibility to help conserve our planet's precious resources. We want to integrate environmental awareness into our strategic decision making and routine work practices, and we are making good progress towards this. With the implementation of the CSR Reporting Manual in 2010 we will be able to start measuring our environmental footprint in a systematic and comprehensive way.

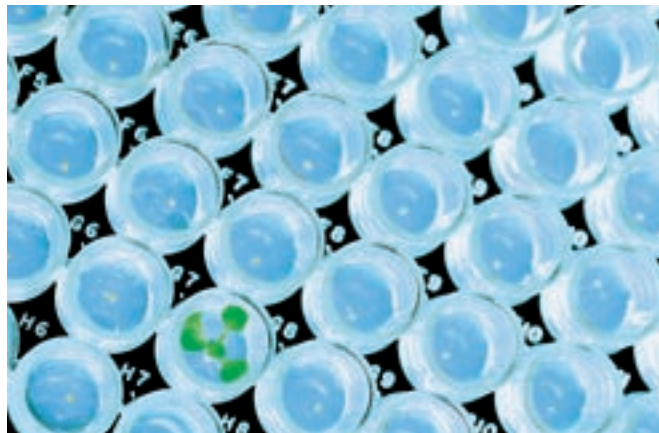
### Sustainable efficiency

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Crucell's introduction of the FlexFactory® (see page 45) has exciting implications for the planet, as well as for our business of healthcare innovation. In this 'lean and green' manufacturing setup, the use of disposable equipment eliminates the need for complicated cleaning and sterilization between production batches. This translates into substantial environmental gains, compared to traditional biopharmaceutical manufacturing in stainless-steel bioreactors. Reductions of 87% in water consumption and 25% in carbon footprint have been calculated.<sup>1</sup>

Less dramatic, but very worthwhile, examples of environmentally friendly initiatives are flourishing throughout the company. Local initiatives of interest include the switch to 100% 'green' electricity in Leiden and the cold box recycling program in Sweden (see the section on responsible supply chain management). The refurbishment of a redundant manufacturing facility in Switzerland is an example of recycling on a large scale.

In other areas, Crucell is leveraging its global reach to achieve sustainable efficiency gains, with spin-off benefits for the environment. In 2009 we have successfully reduced freight, despite growth in vaccine sales, by bundling deliveries and implementing a minimal order policy. Global policies and tools, such as the new procurement policy, will facilitate the choice for green suppliers and rationalize shipments. Crucell used to have a large base of suppliers for a company of our size, which is environmentally wasteful as well as operationally inefficient. This situation, a legacy of Crucell's history as three separate organizations, has successfully been addressed.



In 2009 we pursued our development of 'green' IT through virtualization and more efficient data storage. Use of WebEx and teleconferences rather than travel was encouraged. Our marketing & sales teams made good use of Brand.net, an online platform, to streamline communications with distributors and suppliers: marketing materials can be picked up from the website instead of being sent by post or courier.

### Packaging

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As promised in last year's CSR chapter, we have explored options for improving packaging and initiated changes where possible. For example, the 10-vaccine box of Epaxal®, our hepatitis A vaccine, has been reduced substantially in size. This means we can fit more vaccines on a pallet and make better use of cold chain storage, which is always limited. For this reason, minimizing total storage volume is an important criteria when participating in tenders. This example illustrates how the environment, society and Crucell's business can all benefit from smarter packaging.

Sinclair A, Leveen L, Monge M et al., The Environmental Impact of Disposable Technologies, *Biopharm International*, November 2008.

## Expanding the scope of our ambitions continued

Environmental issues were carefully considered when packaging was being changed in accordance with the Crucell global rebranding. This presented our Regulatory Affairs team with a dilemma, because of the stringent regulations governing healthcare products. Team leader Wolfram Schlimme explains: "We considered using recycled paper for the package inserts, but we had to reject this idea on regulatory grounds. The paper has to be very thin to fit in the smallest possible box, but not transparent as it is printed on both sides. Recycled paper is not strong enough to guarantee that it will not tear—which would lead to recall of the product. Using thicker recycled paper would require a bigger box, and therefore larger cold storage and transport facilities, increased costs and greater energy use. Net result: no environmental gain." This dilemma is a good example of the complexity of factors that must be weighed up in our highly regulated industry. Recycled carton will be used for the new product packaging.

### Energy and water consumption

The first graph on the right shows the total energy consumption in kilowatt-hours (kWh) at Crucell facilities involved in product manufacturing and development, which together employ over 90% of our workforce. A 2.52% decrease in energy consumption in 2009 relative to 2008 can be seen.

Energy use includes electricity, natural gas, oil, and other fuels such as gasoline and diesel, all of which are converted to kWh. Electricity (from the grid) is Crucell's primary source of energy. Crucell's total energy consumption in 2009 is equivalent to that of approximately 3413 average households (which consume 17,906 kWh). In 2008 Crucell's total energy consumption was equivalent to 3502 average households.

The second graph shows the total water consumption in cubic meters at Crucell facilities involved in product manufacturing and development, which together represent

over 90% of our global workforce. A 4.54% decrease in water use in 2009 compared to 2008 can be seen. Dividing the total water consumption by the number of employees allows comparison of annual water use per employee: 194 m<sup>3</sup> in 2009 compared to 221 m<sup>3</sup> in 2008. Crucell's water is sourced from the grid.

### Total energy consumption

(in kWh, million)



### Total water consumption

(in m<sup>3</sup>)





## Philanthropy

Crucell contributes to society in ways that go well beyond its responsibility to discover, develop and market innovative healthcare products. We work proactively and intensively to improve the lives of people worldwide through a broad range of non-commercial activities, which are in line with our core business.

## Community outreach



We are particularly excited by a new Crucell CSR program initiated by our Corporate Communications team in 2009: Footprint. This CSR outreach program offers Crucell employees an

opportunity to contribute in a very direct and practical way to development activities in disadvantaged communities. Groups of Crucell volunteers will participate in projects set up in cooperation with non-governmental organizations (NGOs) and institutions active in the local community. This will ensure that the help given is the help that is really needed. We expect the experience to be equally rewarding for the Crucell employees who take part.

**“Crucell has developed a very promising tuberculosis vaccine candidate which we hope will play a major role in combating the TB epidemic currently afflicting much of the developing world.”**

Associate Professor Willem Hanekom, Co-Director SATVI

After talks with a number of organizations, Crucell has chosen to work with two that are tackling major health challenges in our area of expertise: infectious diseases. One is the South African Tuberculosis Vaccine Initiative (SATVI), which conducts clinical trials of the tuberculosis vaccine Crucell is co-developing with the Aeras Global TB



The Crucell footprint logo painted at a hospital entrance by a SATVI employee to commemorate Crucell's visit.

Vaccine Foundation. The other is Friendship, an NGO that is doing wonderful work to improve access to essential healthcare, such as immunization, in isolated and under-served communities in the Northern part of Bangladesh.

Crucell employees have responded enthusiastically to this special CSR initiative, and the first outreach team was selected from a large number of applicants. The seven participants—drawn from different Crucell sites and departments worldwide—went to South Africa in February 2010. They helped out with a local SATVI community project in Worcester, near Cape Town, and observed child immunization programs in action.

**“We as a TB vaccine trial site are honored to host an outstanding internationally respected collaborator such as Crucell.”**

Dr Hassan Mahomed, Co-Director SATVI

## Expanding the scope of our ambitions continued

Enrique Rioperez, Crucell's Director Finance and Administration in Spain, was one member of the first outreach team. His reaction to that experience sums up the value of this program for Crucell's employees, as well as the communities themselves. "Taking part in Crucell's outreach program 'Footprint' gave me the opportunity to be in touch with the real mission of our organization, the real reason for our existence, the core of our business. It was a great and exciting chance to expand my horizons by learning new things, meeting new people and other cultures. An experience I will never forget!"



### Runa Khan, Executive Director Friendship:

Bangladesh is a 'land of a thousand rivers'. Scattered on these rivers are the 'nomadic islands' or Chars. These lands are migratory, shifting and reappearing across rivers that are often 30 km in width. These islands are home to over eight million people, who live below any documented poverty line. Every year the rivers overflow their banks, bringing 80% of the country under water. For those marooned on the Chars of the rivers Brahmaputra and the Ganges, **survival becomes the goal**. It becomes impossible for them to access the mainland even for food and relief. None have access to healthcare, for themselves or their children.

Here, thousands of children are not receiving the vaccine protection prescribed by the national Expanded Program for Immunization (EPI). Time is running out for meeting the Bangladesh government's Millennium Development Goal target of making EPI services reach 100% of the population by 2015.

Friendship, with the help of Crucell, has made a commitment to ensure that every child on these islands gets the fulfillment of their basic rights to have access to

the EPI services. The Crucell–Friendship EPI support program will assist the government of Bangladesh to provide awareness of the importance of the immunization program to each and every household on these islands, and to carry the services to the population, dependably throughout the year.

The Crucell–Friendship program will develop a river-based infrastructure, using safe boats for regular service delivery, which will be operated jointly with the government health workers. A team of 300 Friendship community medics will be deployed to mobilize the children in the various islands, to increase the acceptance and awareness of inoculations amongst them, and to identify any drop-outs or non-procedural cases. This public-private partnership program will be the first step towards meeting the vision to reduce the mortality and morbidity of vaccine-preventable diseases for children of the Chars—and to help them face their futures with health, strength and courage.



## Crucell and Friendship

Friendship is a value-based national organization dedicated to improving the lives of people living in the remote riverbank and Char areas of northern Bangladesh. The Chars (nomadic islands) are isolated from the mainland in terms of physical distance, access to healthcare, and other basic resources. Outbreaks of infectious diseases are very common, due to high population density, a continuous influx of new infectious agents, and low levels of immunization coverage. Rates of morbidity and mortality due to vaccine-preventable diseases are high, especially among children.

Friendship is endeavoring to help the government improve vaccination coverage in the region by providing support with logistics and infrastructure. Crucell has joined Friendship in this effort, pledging ongoing support for the development of a river-based health service delivery system with floating hospitals, satellite clinics and community medics. Crucell will not only provide financial support for developing this infrastructure and vaccine storage capacity, but also technical expertise and practical help in the field. For example, Crucell employees will provide training in cold chain and vaccine management. "This direct involvement is a very important part of Crucell's commitment, and perhaps the most exciting from the company's point of view," says Oya Yavuz, Crucell's VP Corporate Communications and Investor Relations.

## Supporting government initiatives

Crucell reaches out to communities in need in cooperation with both non-governmental organisations (NGOs) and governments. A good example of the latter comes from our Korean organization. In September 2009, Crucell Korea supplied 14,000 free doses of Inflexal® V, our virosomal influenza vaccine, for use in the national 'Dream Start' program. Dream Start is a government program targeting low-income families. It focuses on preventive healthcare and welfare services in order to break the vicious cycle of poverty from one generation to the next. Children from six months to 12 years received the influenza vaccine at their local Dream Start centre.

## "We reach out to communities in need."

The successful vaccination program triggered the idea of finding other ways to help children attending the Dream Start centers, and involving Crucell employees in these activities. Many of these children live in urban squats and lack access to even basic amenities like hot water, so they do not bathe often. They tend to be rejected by classmates as a result. When Crucell employees heard this, the idea for a fun 'bath day' was born. A group of 20 employees organized a trip to the public baths combined with games, presents and a barbeque. The day was so enjoyable—for children and adults—that the Crucell bath day has become a regular event.

## Vaccine donations

In addition to the donation of Inflexal® V in Korea, Crucell donated 690,000 doses of MoRu-Viraten® vaccine against measles and rubella to Unicef to assist earthquake victims in Haiti. The donation was made as part of the emergency aid campaign organized by the International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), of which Crucell is a member. Crucell also offered 879,000 doses of Hepavax-Gene® to the disaster relief campaign. The offer was under consideration when this report went to press.

## Expanding the scope of our ambitions continued



Crucell Leiden employees gave generously to children's projects supported by the *Stichting Kinderpostzegels* (Foundation for Children's Stamps).

### Raising awareness

The launch of Footprint is part of a coordinated effort to raise awareness of corporate social responsibility (CSR) in our organization. Throughout 2009 this ambition was manifest in many ways. For example, our Christmas present for employees (see image below) was a responsible choice: a leather-bound notebook designed and made exclusively for Crucell by local craftspeople in Dhaka, Bangladesh. We ran a global photo competition linking the theme of CSR to The Crucell Ambition—and discovered how active some of our employees are in local volunteer work. Our employees in Leiden gave generously to fundraisers for good causes, including the Red Cross fight against malaria and children's projects supported by the *Stichting Kinderpostzegels*. Crucell management doubled their contribution.



### Access to healthcare

Crucell's work with Friendship is an example of a targeted local initiative to solve problems of access to essential healthcare. Crucell also works on this issue at the global, international and national level, through close and continuous engagement with a wide range of government and non-governmental organizations. Examples of our involvement in 2009 are as follows.

- Crucell was the vaccine industry representative on the formal advisory Program & Policy Committee of the GAVI Alliance, a public-private partnership with the mission to improve access to vaccines in the world's poorest countries. In 2009, this advisory committee focused on issues such as support eligibility and continuity, strengthening health systems and building capacity, the sustainability of established programs, and the conditions on which GAVI should accept vaccine donations.
- Crucell contributed, as a member of the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) Biologicals & Vaccines Committee, to discussions with the World Health Organization (WHO) on general vaccination policies.
- Crucell served on the advisory group for Project Optimize, a WHO/PATH collaboration aimed at developing innovative delivery systems to ensure that vaccines get to the right place, at the right time, in the right condition. Crucell's representative on the advisory group presented the issues of vaccines and cold chain management to a broad audience at the GAVI Partners' Forum in Vietnam. Crucell's participation in this advisory group is ongoing.
- Crucell is a member of the European Vaccine Manufacturers (EVM), part of the European Federation of Pharmaceutical Industries and Associations, which is committed to working in partnership with EU institutions to support vaccine policy development and promote vaccine innovation. Crucell representatives serve on the



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**In 2009 Crucell participated in 37 global scientific conferences and events.**

EVM board and task forces. In 2009 this group focused on developing the concept of life-course vaccination (vaccine policies for all ages, a highly relevant issue because of aging populations), pandemic influenza and market access in Europe.

- Crucell has been instrumental in bringing together the worldwide stakeholders in the field of typhoid fever with an ultimate goal of creating a Coalition against Typhoid (CaT) that will have its leadership in the Sabin Vaccine Institute in Washington, DC.

## Contributing to science

Crucell contributes to the advancement of science and healthcare by sharing knowledge and expertise. In 2009 Crucell participated in 37 global scientific conferences and events, and many more informal meetings and media presentations. As in previous years, Crucell organized symposia during 2009, to facilitate information exchange among key opinion leaders and public health officials. A total of 29 scientific papers by Crucell researchers were published in peer-review journals in 2009.

As the pandemic (H1N1) 2009 influenza virus emerged, Crucell was part of the expert community examining the evolving situation, in terms of viral transmission and pathology, and helping to guide appropriate action. One way in which we did so was through our regular meetings with SAGE (Strategic Advisory Group of Experts), the principal advisory group to the World Health Organization (WHO) for development of policies related to vaccines and immunization.

Crucell also assisted non-governmental organizations (NGOs) doing early research into the pandemic (H1N1) 2009 influenza virus strain. For example, we supplied serum samples from seasonal flu vaccination campaigns in past years to assist research by the National Institute for Biological Standards and Control (NIBSC) in the UK, one of four WHO reference centers. The NIBSC wanted to determine whether antibodies generated by vaccines against previous seasonal influenza strains provide cross-protection against the pandemic virus. The finding that there is some degree of cross-protection in older populations has helped to guide thinking about who should be vaccinated against the pandemic (H1N1) 2009 influenza virus.

## Sector sustainability initiatives

As mentioned in section 2 of this CSR chapter (Transparency: Developing our approach to CSR) Crucell has taken significant steps to define and develop its commitment to sustainability issues. Crucell's listing on the Dow Jones Sustainability Index in 2009 is one objective measure of this. Continuing this development is one of Crucell's CSR ambitions for the years ahead.





## Expanding the scope of our ambitions continued

### The way forward: Our CSR ambitions, targets and tools

Crucell is committed to developing a systematic approach to CSR performance and reporting. We see the value of embedding a mature CSR mind-set and methodology in our global organization, and we are taking concrete steps towards this goal. In this section we outline the contours of our ambitions for the coming years and our strategy for achieving these ambitions. An initial set of key performance indicators and targets is presented.

#### Better insight

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Improving the collection and analysis of CSR-related data is Crucell's immediate priority and one of our main ambitions for CSR development. Without a comprehensive overview of our impact on society, we cannot hope to maximize the good we do while minimizing any adverse effects. That is our overriding ambition relating to CSR. Better information management is simply the means to that end.

Over the past two years, Crucell has made important progress in the development of global systems in many areas, including information management. This is a direct result of our intensive efforts to build a fully integrated, global biopharmaceutical company following the acquisition of the Swiss concern Berna Biotech and Swedish company SBL Vaccines in 2006. In the areas of environment, health and safety (EHS), for example, we now have access to solid data from our five main sites worldwide, representing over 90% of our workforce (comparable with the reporting coverage in the 2008 Annual Report CSR chapter).

While these data give us a substantial base for initial CSR target setting, they obviously do not provide the full picture needed for optimal CSR development. Achieving 100% information coverage (that is, data from all sites) is therefore one of Crucell's most important short-term ambitions. This is one of the targets set for 2010. At the end of the year we want to have a complete picture of information relevant to our CSR ambitions, collected in the same way, using the same criteria and definitions.

To achieve this goal, we are currently developing the infrastructure needed for centralized management of all the information relevant to CSR. This 'Reporting Manual' with instructions, criteria and a reporting tool will be rolled out in 2010.

#### Continuous improvement

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Once we have established our CSR baseline, with 100% coverage across sites, we will be able to perform quantitative analyses to identify possible improvements—for example, in EHS and the responsible management of our supply chain. This will enable quantitative target setting for the longer term. Table 2 gives an overview of our main ambitions relating to CSR.

Crucell's Management Board has taken the ambitious step of formulating longer-term objectives in several areas. These are challenging targets: in 2020 a 15% reduction (from 2010 baseline) in our CO<sub>2</sub> footprint and a 10% reduction in water use, and in 2015 reaching a high standard of CSR transparency as measured by the Global Reporting Initiative (GRI) A level. Based on data collected within Crucell and comparison with others in the industry, we see these as ambitious but achievable targets.

**Table 2**

Ambition	2010	2011	Long term
CSR information management improvement	Roll out Reporting Manual & report based on 100% company coverage	Quantitative ambition setting (EHS)	
Transparency objectives	Remain in DJSI <sup>1</sup> & improve CSR webpage	Continuous improvement	2015: GRI <sup>2</sup> A rating
Responsible supply chain	Extend global procurement policy	Training, 100% information coverage & monitoring	
CO <sub>2</sub> Footprint	Baseline setting	Quantitative ambition setting	2020: 15% reduction
Water use	100% company coverage (reporting)	Quantitative ambition setting	2020: 10% reduction

<sup>1</sup>DJSI – Dow Jones Sustainability Initiative, <sup>2</sup>GRI – Global Reporting Initiative



Ambitions and targets will be reviewed annually and finetuned as new information generates deeper insight into the potential for improvement. Crucell's Management Board will closely monitor progress and expand Crucell's CSR ambitions if opportunities to do so become apparent. Thus, Crucell's approach to CSR development will follow the principle of continuous improvement, which is fundamental to our corporate culture and business strategy.

Crucell has defined KPIs and ambitions in each of the four categories on which our CSR policy is based: Performance, People, Planet and Philanthropy. These are presented in the following paragraphs.

**“Crucell is committed to developing a systematic approach to CSR performance and reporting.”**

## Expanding the scope of our ambitions continued

### Performance

The category 'Performance' covers the four aspects of CSR that relate most directly to Crucell's core business: innovation, saving lives, responsible supply chain and transparency. Table 3 shows the qualitative or quantitative ambitions we have in these Performance areas and the KPIs we have chosen to assess achievements in each of these areas. The reasoning behind these choices is explained below.

**Preventing illness and death** caused by infectious diseases is our core business, and the essence of our corporate social responsibility. The prevention of deaths is the most powerful measure of the human benefit generated by our business, and our ambition is to continuously increase this impact. The calculation is based on the best available evidence regarding the efficacy of our vaccines, and the relevant disease and death rates in unvaccinated populations.

**The number of products in our research & development (R&D) pipeline** is a measure of the contribution we are making to people's lives through the advancement of healthcare. Crucell deliberately focuses on the discovery and development of innovative products—vaccines and antibodies—that address significant unmet needs in global health.

**Animal Welfare.** Crucell will continue to apply the 3R principles – Reduce, Refine and (ultimately) Replace – and work closely with the regulatory authorities to further minimize the experimental use of animals in the course of bringing new vaccines and antibodies to the people who need them.

**“Improving CSR information management is a prerequisite for increasing the contribution we can make to society.”**

**R&D expenses.** The money Crucell spends on its R&D programs is a measure of the company's commitment to invest in bringing healthcare innovations to market, and to do so as cost-effectively as possible. As announced in our financial guidance for 2010 (see press release on 2009 financial results, 9 February 2010), Crucell is focusing strongly on accelerating product development. Strong operating cash flow will be used to increase research & development spending by more than one-third in 2010 compared to the previous year.

**Improving CSR information management** is a prerequisite for increasing the contribution we can make to society. Having access to comprehensive information on relevant KPIs in 2010 will enhance further target setting.

**Table 3**

Performance	Qualitative	Quantitative	Ambition/Target
Prevention of illness and deaths	•	•	Continuous improvement, report annually
Number of pipeline products	•		Report annually
Animal welfare	•		Continuous improvement 3Rs
R&D expenses		•	Report annually
CSR information management improvement	•		<ul style="list-style-type: none"> <li>• In 2010 roll out reporting manual</li> <li>• In 2010 report with 100% company coverage</li> <li>• In 2011 set action plans (quantitative targets)</li> </ul>
Responsible supply chain		•	<ul style="list-style-type: none"> <li>• In 2010 incorporate PSCI<sup>1</sup> principles into procurement policy</li> <li>• In 2011 train all relevant employees</li> <li>• In 2011 100% supplier coverage &amp; monitoring</li> </ul>
Transparency objectives (e.g. DJSI <sup>2</sup> , CDP <sup>3</sup> , GRI <sup>4</sup> )		•	<ul style="list-style-type: none"> <li>• GRI A+ level CSR reporting in 2015</li> <li>• Remain in DJSI</li> <li>• In 2010 improve CSR webpage</li> </ul>

<sup>1</sup> PSCI – Pharmaceutical Supply Chain Initiative, <sup>2</sup> DJSI – Dow Jones Sustainability Initiative, <sup>3</sup> CDP – Carbon Disclosure Project, <sup>4</sup> GRI – Global Reporting Initiative



## Expanding the scope of our ambitions continued

**Responsible supply chain management.** The prerequisite for progressive improvement in this area has been achieved in 2009 with the professionalization of our procurement organization. The next step, for realization in 2010, is to incorporate industry best practices for responsible supply chain management, as defined by the Pharmaceutical Supply Chain Initiative, into our global procurement policy. The ambition for 2011 is to train all relevant employees in this procurement policy and ensure that all suppliers adhere to it. In addition, monitoring of relevant developments in the sector is targeted, so that ambitions and indicators can be refined, if necessary.

**Transparency objectives.** Crucell has recently made very good progress on external benchmarks of CSR reporting, as described on page 41. Our ambition is to continue this rapid improvement. We have set the challenging target of reaching the Global Reporting Initiative 'A' level of CSR transparency in 2015.

**“Attracting and retaining talented employees is an ongoing priority.”**

### People

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Crucell has made significant progress over the past two years in the area of Human Resources (HR) management and talent development. Global integration, leadership development and performance assessment procedures have been given special attention during this period, and turnover has decreased considerably (see page 52). Expanding career and learning development opportunities for all employees will be a focus during 2010.

In terms of CSR reporting, our ambition in 2010 is to formulate specific targets for each of the KPIs (see table 4). The choice of these particular KPIs reflects Crucell's commitment to being an employer of choice.

**Demographics.** We value and support diversity—of culture, gender and age—in our organization. The relatively low number of women in senior management positions is a point for attention. However, Crucell is committed to recruiting and promoting employees on the basis of talent and ability, without negative or positive discrimination on the basis of gender, race or age.

**Accidents.** The health and safety of our employees is of great importance to us, and we take proactive steps to enhance these. Achieving more comprehensive and detailed information on accidents at work is a priority for 2010 and a prerequisite for future target setting.

**Turnover.** Attracting and retaining talented employees is an ongoing priority. We see turnover as a key indicator of how well we are doing in this regard.

**Empowerment and fairness.** Crucell is committed to fair remuneration and the empowerment of employees, for example through regular performance reviews.





**Table 4**

People	Qualitative	Quantitative	Ambition/Target
Number of employees by gender	•		Formulate target in 2010
Average age of employees	•		Report annually
Number of women in management	•		Formulate target in 2010
Number of nationalities	•		Formulate target in 2010
Total number of accidents	•		Formulate target in 2010
Employee turnover	•		Formulate target in 2010
% employees receiving regular performance reviews	•		Formulate target in 2010

## Expanding the scope of our ambitions continued

### Planet

Thanks to improved collection of environmental data in 2009, Crucell has been able to formulate long-term ambitions and targets for reducing water use and its CO<sub>2</sub> footprint. Comprehensive measurement of these KPIs across all sites in 2010 will establish the baseline against which progress will be measured in subsequent years and allow finetuning of targets. Targets for health and safety measures (accidents and waste disposal) will be formulated in 2010 as better data management enables meaningful analysis.



Table 5

Planet	Qualitative	Quantitative	Ambition/Target
Total water use		•	<ul style="list-style-type: none"> <li>• Relative reduction* of 10% by 2020</li> <li>• In 2010 achieve 100% coverage (i.e. baseline)</li> </ul>
Total energy use		•	<ul style="list-style-type: none"> <li>• See CO<sub>2</sub> Footprint</li> <li>• In 2010 achieve 100% coverage</li> </ul>
CO <sub>2</sub> Footprint		•	<ul style="list-style-type: none"> <li>• Relative reduction* of 15% by 2020</li> <li>• In 2010 set baseline</li> <li>• In 2011 set action plans</li> </ul>
Number, sort and impact of accidents	•		Formulate target in 2010
Amount and characteristics of waste and disposal method	•		Implement waste minimization programs on all sites

\*Relative to number of FTEs

Philanthropy

As a company deeply committed to improving human health and well-being, Crucell actively seeks out opportunities to do more for society than it ‘needs’ to do from a business point of view. These efforts span a wide range of activities, from sharing scientific knowledge to supporting the development of local communities. Improving access to healthcare, especially in the world’s poorest countries, is a high priority. We do that by working with governments, non-governmental organizations (NGOs), policy makers, industry groups and public–private partnerships such as the GAVI Alliance, as well as local community groups. Our ambition is to continue our involvement in a broad spectrum of philanthropic activities, and to report on these efforts in a transparent way.



Table 6

Philanthropy	Qualitative	Quantitative	Ambition/Target
Number of doses donated	•		Report annually
Support of sector initiatives	•		Further Crucell involvement
NGO partnerships	•		Liaise with key NGOs and evaluate partnership yearly

CSR infrastructure

- To support the embedding of CSR in the organization, Crucell has established the following responsibilities and procedures.
- Ronald Brus, Chief Executive Officer, has final responsibility for Crucell’s CSR program and its ongoing development.
  - Cees de Jong, Chief Operating Officer, has overall responsibility for operational aspects of the CSR program.
  - A CSR working group will be established to monitor and facilitate CSR development.
  - Progress on the CSR program will be discussed at Management Board meetings.
  - The CSR working group will meet at least two times a year to discuss CSR development and evaluate progress.

Conclusion

Corporate social responsibility (CSR) is an integral part of Crucell’s mission to conduct good business, for the good of humanity. Crucell is committed to continuous development of its approach to CSR reporting and the engagement of stakeholders in dialogue about sustainability issues. We are pleased to have taken important steps in this direction during 2009.

Crucell welcomes feedback on this report or any issues related to our CSR activities. Your opinion matters to us. Reactions can be sent to [csr@crucell.com](mailto:csr@crucell.com).

# Forward-looking statements/Trademarks

## Forward-looking statements

This Annual Report contains forward-looking statements. All statements regarding our future financial condition, results of operations and business strategy, plans and objectives are forward-looking. Statements containing the words 'believes', 'intends', 'expects', and words of similar meaning are also forward-looking. In particular, the following are forward-looking in nature: statements with regard to strategy and management objectives; technology and product development efforts; our ability to realize commercially valuable discoveries; our intellectual property portfolio; our ability to develop potential products and technologies suitable for commercialization; the effects of changes or prospective changes in regulation; and trends in results, operations and overall market trends.

These forward-looking statements involve risks, uncertainties and other factors, some of which are beyond our control, that may cause our results, performance or achievements or conditions in the markets in which we operate to differ from those expressed or implied in these forward-looking statements. We describe certain of these risks and uncertainties in the section 'Risk factors'. We caution not to place undue reliance on these forward-looking statements, which reflect our Management's view only as of the date of this document.

## Trademarks

New trademarks for our products are registered on a worldwide basis. Distribution and agency agreements normally include a clause specifying that, at the termination of the agreement, trademark and product registration rights return to us. We are the owner of over 150 registered trademarks. The most important of these are: CRUCELL®, BERNA®, SBL®, the Berna, SBL and Crucell logos, ChromaGenics®, EPAXAL®, Epaxal® Junior, INFLEXAL®, VIVOTIF®, FLAVIMUN®, DUKORAL®, HEPAVAX-GENE®, MoRu-Viraten®, PER.C6®, PER.C6® logo, AdVac®, MAbstract® and STAR®. In addition we hold rights to use certain trademarks that are owned by our partners, such as Quinvaxem® from Novartis. All other trademarks, service marks, trade names and registered marks used in this report are trademarks, trade names or registered marks of their respective owners. Crucell N.V. and its subsidiaries own a number of additional trademarks, including registered trademarks that are not referenced in this report.

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All amounts set forth in this Annual Report, unless otherwise noted, are in thousands of Euro, except share and option data.

# Report of the Management Board

## Overview of the year

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The global financial crisis dominated world news in 2009, but for Crucell it was a year of record sales and profits. We exceeded our revenue targets and generated a strong operating cash flow in 2009, building on our strong performance in 2008. Delivering on promises is an important aspect of The Crucell Ambition, our corporate strategy, and we are excited to have delivered even more than we promised at the start of the year. Highlights of our financial performance in 2009 are:

- Total revenues and other operating income increased 26% to € 358.0 million.
- Operating profit increased more than four-fold to € 39.0 million.
- Net profit increased 68% to € 23.9 million.
- Undiluted earnings per share increased 55% to € 0.34.
- Year-end cash and cash equivalents totaled € 327.8 million in 2009, compared to € 171.0 million in 2008.

The single most important event of the year was the signing of a strategic agreement with affiliates of Johnson and Johnson (JNJ) in September 2009. This agreement will enable us to accelerate and expand our research and development (R&D) programs while maintaining Crucell's independence and autonomy. The agreement with the affiliates of JNJ is a strong endorsement of Crucell's in-house capabilities for medical innovation and discovery.

Crucell issued 14.6 million shares to JHC Nederland B.V., an affiliate of JNJ, at a price of € 20.63 per share, for a total of € 301.8 million. This represents 18% of our outstanding share capital after issuance. As part of the agreement with Ortho-McNeil-Janssen Pharmaceuticals, Inc, an affiliate of JNJ, we will jointly develop and commercialize a novel monoclonal antibody product for the treatment and prevention of influenza, regardless of the causal strain. The collaboration also involves new discovery programs aimed at the development and commercialization of a universal influenza vaccine as well as innovative products in up to three other disease areas.

The agreement with the affiliates of JNJ has substantially reduced the risks inherent in our business by providing a solid operational framework with one of the largest pharmaceutical companies worldwide.

## Business drivers

Our strategy is based on the following business drivers:

- A strong R&D pipeline with promising products in a range of major disease areas;
- Licensing of cutting-edge technologies that enable the discovery, development and production of biopharmaceutical products;
- A broad range of vaccine products that combat important infectious diseases.

## Strong R&D pipeline

During 2009, we made substantial progress with our R&D programs, which are targeting innovative solutions for a number of major health challenges.

Crucell's influenza antibody research is still at an early stage but shows tremendous promise. As reported previously, Crucell's scientists have discovered a new class of human monoclonal antibodies with the unprecedented ability to combat a broad range of influenza virus strains. The most powerful of these antibodies has been shown to prevent and cure illness in pre-clinical models exposed to potentially lethal levels of H5N1 and H1N1 viruses. In comparative pre-clinical tests, this antibody strongly outperformed oseltamivir (Tamiflu), the leading antiviral treatment available today. The discovery and characterization of this unique class of human influenza antibodies was reported in the online journal PloS ONE on 16 December 2008 and Science on 26 February, 2009.

The exciting therapeutic potential of this discovery has attracted global leaders in healthcare innovation. The development and commercialization of a universal antibody product against influenza (flu-mAb) is the immediate focus



of the collaboration between Crucell and JNJ, signed in September, 2009. The agreement followed an announcement in August 2009 of an award from the National Institute of Allergy and Infectious Diseases (NIAID), part of the US National Institutes of Health (NIH). The NIAID award, designed to support early development of Crucell's influenza mAbs, provided initial funding of up to \$ 40.7 million, with additional options worth a further \$ 28.4 million, bringing the potential total funding to \$ 69.1 million.

Promising results from a Phase II clinical study of Crucell's rabies monoclonal antibody combination, conducted in healthy children and adolescents in the Philippines, were released in June 2009. As well as confirming that our candidate antibody product against rabies is safe and well-tolerated in the young—the group at greatest risk of infection—the study delivered strong evidence of efficacy. All study participants achieved adequate levels of immunity and the same level of protection against rabies that is achieved with human immunoglobulins (HRIG), the current standard for inducing immediate, passive immunity. An additional Phase II clinical study is scheduled to start in India during 2010. The rationale for this study is to collect data on the safety and efficacy of our candidate rabies product in a simulated setting of rabies post-exposure prophylaxis (prevention). This will pave the way for a Phase III trial in a real prophylactic situation.

The candidate tuberculosis vaccine we are co-developing with Aeras Global TB Vaccine Foundation entered its first trial in infants in April 2009. The main objective of this Phase I clinical trial is to test the safety of the candidate vaccine in infants previously vaccinated with BCG vaccine, currently the only licensed vaccine against tuberculosis. BCG vaccine shows limited efficacy when used alone. The South African Tuberculosis Vaccine Initiative (SATVI) is conducting this Phase I trial among infants in the Western Cape region of South Africa. The study is fully enrolled and dosing is ongoing, with no safety issues identified to date. In January 2010, a Phase I clinical trial was initiated in Portland, Oregon, USA. This trial involves the vaccination of healthy adults with a known immunogenic regimen of BCG and the candidate vaccine, followed by collection of large numbers of immune cells to enable more detailed analysis of the immune response to candidate vaccine.

In July 2009, we announced a new collaboration with the US-based Malaria Vaccine Initiative (MVI) and the US Agency for International Development—Malaria Vaccine Development Program (USAID MVDP) to accelerate development of a promising new type of malaria vaccine. Through funding from the USAID MVDP, the partners will conduct studies to determine the effectiveness of Crucell's novel prime–boost vaccine approach against the malaria parasite *Plasmodium falciparum*. Using Crucell's AdVac technology, with two different adenovirus vectors (Ad35 and Ad26) as delivery mechanisms, this approach seeks to elicit a protective immune response to the circumsporozoite protein (CSP).

We are also pleased with developments in our HIV research program. At the international AIDS vaccine congress held in Paris in October 2009, we presented encouraging preliminary results of a Phase I study of the novel HIV recombinant AdVac-based vaccine Crucell is co-developing with the Beth Israel Deaconess Medical Center (Boston, Massachusetts, USA). This innovative vaccine uses adenovirus serotype 26 as a vector in order to avoid pre-existing immunity to the more commonly used adenovirus serotype 5. The Phase I clinical study is being conducted at the Brigham and Women's Hospital in Boston. The preliminary results indicate that the candidate HIV recombinant AdVac-based vaccine is safe and immunogenic—news that was received with enthusiasm by the international AIDS community.

In August 2009, Crucell obtained an exclusive license from Stanford University (Palo Alto, California, USA) for the development of antibodies against the hepatitis C virus (HCV). Crucell is evaluating a large panel of fully human monoclonal antibodies against HCV in a proof of concept phase.

During 2009, we also advanced research aimed at developing a multivalent filovirus (Ebola and Marburg) vaccine based on Crucell's innovative AdVac and PER.C6 technologies. An Ebola vaccine using adenovirus 5 (Ad5) as vector, which Crucell is developing in partnership with the NIAID/NIH Vaccine Research Center, showed safety and immunogenicity in a Phase I study. Based on these results, a second Phase I study of an Ebola and/or Marburg vaccine is anticipated. This will use alternative multivalent adenovirus vectors that are able to bypass pre-existing immunity against Ad5.

Crucell's yellow fever vaccine Flavimun was submitted for registration in Switzerland in the first quarter of 2009.

## Report of the Management Board continued

### Licensing of cutting-edge technologies

License revenues in 2009 were € 23.0 million, representing a decrease of € 7.2 million (23.7%) compared to the previous year. The decrease is mainly due to € 14.0 million in one-off milestone payments from sanofi pasteur in relation to our rabies development program in 2008. License revenues in 2009 include significant payments associated with our JNJ collaboration and royalty payments from Shanta, an Indian vaccine manufacturer.

In 2009 Crucell signed 12 new licensee/ vendor agreements pertaining to Crucell technology, including agreements with Centocor Inc., Momotaro-Gene Inc., Patrys Ltd., TapImmune Inc., Calmune Corporation, Cangene and Vivante GMP Solutions. Vendor Network Agreements were signed with Bioceros B.V. and KBI Biopharma Inc.

For further details on licenses and licensees please see the 'Appendix overview licensees and partners' in this Annual Report.

### Broad range of vaccine products

Product sales for the full year 2009 were € 304.4 million, representing sales of paediatric vaccines (59%), travel and endemic vaccines (18%), respiratory vaccines (12%) and other products (11%). Compared to 2008, product sales grew by € 78.4 million (34.7%) in 2009. The increase is primarily due to growth in sales of our paediatric vaccines (increase of € 69.4 million or 62.5% compared to the previous year), respiratory vaccines (€ 5.6 million or 17.2% higher than 2008) and other products (an increase of € 5.9 million or 22.0%).

Quinvaxem is our fully liquid vaccine against five major childhood diseases. In 2008 we more than doubled production of this life-saving vaccine and we were able to build on that increase in 2009. Sales of Quinvaxem have risen from 21.3 million units in 2007 to 39.6 million units in 2008 and 64.3 million units in 2009.

Quinvaxem has been pre-qualified by the World Health Organization (WHO) and is therefore available for purchase

by supranational organizations. These organizations are major customers for combination vaccines, which are used in mass-vaccination programs around the world. In August 2009, we announced a long-term arrangement with UNICEF to supply up to \$ 300 million worth of Quinvaxem for the period beginning 2010 through 2012. The new arrangement is the largest ever received by Crucell. With only half of the tendered volume for the 2010–2012 period awarded to date. Revenues are expected to grow further during the contract period. The new arrangements are in addition to the \$ 500 million received during the 2007–2009 period.

In September 2009, we launched our own marketing & sales operations in the United Kingdom by acquiring an experienced team of marketing & sales personnel. This move is in line with our targeted strategy for optimizing sales in high-potential markets. We expect that these operations will further strengthen our vaccine sales position in the United Kingdom, one of the largest travel vaccine markets in Europe. Marketing of our travel vaccines Epaxal, Vivotif and Dukoral has commenced and is progressing well. Sales of our virosome vaccine against seasonal influenza will start prior to the beginning of the 2010 flu season in the second half of the year.

In November 2009, we announced the launch of a consistent identity – a Global Brand - for our worldwide activities and products. The rebranding reflects the successful integration of the historically separate companies making up today's Crucell. It is designed to promote recognition of the Crucell name and what it stands for: bringing meaningful innovation to global health, with a focus on combating infectious diseases. The establishment of a strong global brand will significantly support this mission.

### Operations

We recruited more than 120 new employees during 2009, mostly for our R&D departments in Leiden and Bern. Many of these new colleagues will be working in Switzerland, in the two buildings that were modified in 2009 specifically for the development of our candidate tuberculosis vaccine and

activities necessary to achieve registration of our hepatitis A vaccine Epaxal in the United States.

Construction of our new manufacturing facility for Quinvaxem and Hepavax-Gene in Korea has progressed extremely rapidly since we announced our intention to relocate from the Shingal site in Yongin City to the Incheon Free Economic Zone. Building started in December 2008 and the first test runs in the new plant are planned for the second quarter of 2010. The new facility will enable further increases in productivity and efficiency, ensuring that production of our pentavalent and hepatitis B vaccines continues to meet growing demand. The investments in the new facility are expected to total approximately € 50 million, with the majority of spending made in 2009.

All our facilities were audited several times during the year by customers and/or regulatory authorities. All audits were successful, confirming our compliance with relevant rules and regulations. Our Vivotif production line in Bern, Switzerland, was inspected and approved by the US Federal Drug Administration (FDA). In Madrid, Spain, we installed a new filling line for Epaxal and Inflexal V, bringing the total capacity of our dedicated fill/ finish center in Spain to approximately 100 million syringes per annum. The new filling line was used to prepare syringes of Inflexal V for the 2009 flu campaign.

In August 2008, we announced the intention to move Dukoral and rCTB bulk production, formulation and fill/finish activities from Sweden to other Crucell sites. Following a study to review the full scope of this move, we took the decision in May 2009 to move only the formulation, filling and packaging activities to our Madrid site.

#### **Other**

On January 7, 2009, we announced that we were in friendly discussions with Wyeth regarding a potential combination of the two companies. Wyeth's withdrawal from these discussions was announced on January 26, 2009.

#### **Subsequent events**

On March 8, 2010 Crucell announced that Jerald C. Sadoff, MD was appointed Chief Medical Officer at Crucell and will be a member of Crucell's Management Committee. Before joining Crucell Dr. Sadoff worked at the Aeras Global TB Vaccine Foundation, where he became President and Chief Executive Officer in June 2003. Throughout his career,

Dr. Sadoff has chaired or served on over 20 national and international task forces, initiatives, consulting groups and advisory boards. Currently, he is Chair of the USAID Malaria Vaccine Scientific Consultants Group and Chairs several Scientific Advisory Boards for NIH sponsored HIV vaccine efforts.

On March 15, 2010 we announced that Mr. William (Bill) Burns, Mr. James Shannon and Mr. George Siber are nominated to join our Supervisory Board. The Supervisory Board of Crucell has nominated Mr. Burns, Mr. Shannon and Mr. Siber as new members of the Board, to be presented to our shareholders at the Company's annual general meeting of shareholders on June 4, 2010.

Mr. Burns (1947), a British national, has built a distinguished track record in the pharmaceutical industry over the last 40 years. Most recently Mr. Burns served as the CEO of the Pharmaceuticals Division of Roche.

Mr. Shannon (1956), a British national, with over 20 years of experience in senior development positions, most recently served as Head of Global Development at Novartis Pharma AG in Basel. At present Mr. Shannon holds the position of President and CEO of Cerimon Pharmaceuticals, Inc. and serves on the Boards of Arch Therapeutics; Endocyte Inc; Mannkind Corporation and Xanodyne Pharmaceuticals, Inc.

Mr. Siber (1944), an American national, is regarded to be one of the leading global authorities in vaccines. Mr. Siber currently serves on numerous advisory committees including those of the PATH's Pneumococcal Vaccine Project, MVI, the Gates Maternal Immunization Program, the Stop TB Task Force and the Scientific Advisory Board of several vaccine companies, including Novartis Vaccines and Diagnostics, LigoCyte Pharmaceuticals, Inc. and Variation Biosciences.

On April 6, 2010, Crucell announced that it has signed a binding letter of agreement with GlaxoSmithKline Biologicals (GSK) to collaborate on developing a second generation malaria vaccine candidate. Under the terms of the letter of agreement, we will contribute our recombinant malaria vaccine candidate, Ad35-CS, based on our PER.C6 and AdVac technologies and GSK will contribute its late stage malaria vaccine candidate RTS,S/AS.

# Report of the Management Board continued

## Outlook 2010

Performance versus outlook

We met and exceeded all financial targets set in our outlook for 2009.

	Target 2009	Reported 2009
Revenue and other income <sup>1</sup>	20% growth	29% growth
Operating profit	significantly improved	€ 39.0 million
Cash flow	Solid	+ € 156.9 million

The weakness of the global economy in 2009 was a challenge for many companies worldwide and has adversely affected businesses in many industries and geographical areas all over the world. Despite this difficult economic climate, we not merely achieved but surpassed all targets we had set for the financial year 2009. Our resilience depends in part on our solid customer base, which is relatively unaffected by deterioration in the global economy, since many of our customers are governmental agencies or supranational organizations. It also reflects adherence to the clear priorities set as part of The Crucell Ambition strategic program, which is designed to promote the development of our organization and people, operational excellence, strategic focus and delivery on promises.

## Outlook 2010

We confirm the outlook as provided to the market on February 9, 2010:

- Continued strong operating cash flow to accelerate product development;
- R&D spending to increase by over one-third;
- Maintaining a healthy operating profit;
- Revenues and other operating income broadly in line with 2009<sup>2</sup>.

<sup>1</sup> In guidance currencies = EUR/USD rate of 1.35

<sup>2</sup> In guidance currencies = EUR/USD rate of 1.41

We can look back on 2009 as a year of unprecedented success in terms of both financial performance and strategic alliances. In particular, our landmark agreement with JNJ is a springboard for achieving our ambition to become a world leader in healthcare innovation. We embark on the new decade better equipped than ever to face the challenges and seize the opportunities of the future.

# Information on the Company

## History and development of Crucell

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We are a public limited liability company under Dutch company law, incorporated in Leiden, the Netherlands with the legal and commercial name Crucell N.V. (the 'Company'), registered under number 28087740. We were incorporated on October 9, 2000, as the holding company for Crucell Holland B.V., formerly called IntroGene B.V., following the combination of IntroGene B.V. and U-BiSys B.V. Our principal executive office is located at Archimedesweg 4-6, 2333 CN Leiden, the Netherlands. Our telephone number is +31 (0)71 519 9100. Our registered agent in the US is CT Corporation, 111 Eighth Avenue, New York, New York 10011. The Company and its subsidiaries together constitute the Crucell Group, or the 'Group'. The Company has subsidiaries in the Netherlands, Switzerland, Spain, Italy, Sweden, the UK, Korea and the US.

In February 2006, we acquired a controlling interest in the Swiss biotech company Berna Biotech AG in a share exchange. In September 2006, we acquired the remaining 1.6% minority interest. Berna Biotech AG was founded in 1898. Prior to the acquisition, Berna was a fully integrated biotechnology company that marketed numerous vaccines on a global scale.

In October 2006, the Company purchased, via its subsidiary Crucell Vaccines Inc., the assets and liabilities of the Florida-based Berna Products Corp. from Acambis plc. Berna Products Corp. was originally established in 1990 by Berna Biotech AG to market Vivotif, Berna's oral typhoid fever vaccine, in the US and Canada and was acquired by Acambis plc in 2003.

In November 2006, we acquired the shares of Stockholm-based SBL Vaccin Holding AB (SBL) from 3i and SEB. SBL was a fully integrated independent Swedish biotechnology company. SBL's main product was Dukoral. In addition, SBL had a sales and distribution organization for vaccines in Scandinavia.

In November 2006, we and our technology partner DSM Biologics opened the PERCIVIA PER.C6 Development Center in Cambridge, Massachusetts, US. The joint venture was conceived and designed to further develop the PER.C6 cell line and provide turnkey solutions for the production of monoclonal antibodies and recombinant proteins.

On June 5, 2009 the Group established Crucell UK Ltd. On July 15, 2009 the Group purchased, via its subsidiary Crucell UK Ltd., selected assets and liabilities of UK-based Masta Ltd. The relevant assets acquired in the business combination pertained to the customer base and workforce of the UK fields activities of Masta Ltd.

In September 2009 JNJ, through its subsidiary Ortho-McNeil-Janssen Pharmaceuticals, Inc., purchased 14.6 million newly issued ordinary shares of Crucell, representing approximately 18% of the Company's outstanding ordinary shares (after issuance), for an aggregate purchase price of € 301.8 million. In addition we entered into a strategic collaboration with JNJ focusing on the discovery, development and commercialization of monoclonal antibodies and vaccines for the treatment and prevention of influenza and other infectious and non-infectious diseases.

In November 2009, Crucell announced the launch of the global Crucell brand, a consistent identity for its worldwide activities and products. The rebranding is designed to promote recognition of the Crucell name and what it stands for: bringing meaningful innovation to global health, with a focus on combating infectious diseases. As part of this process the legal names of a number of our subsidiaries were revised. See note 1.1 'Corporate information' in the notes to the financial statements for a complete overview of these changes.



# Information on the Company continued

## Overview

The chapter ‘Information on the Company’ provides an overview of the market we operate in, our business drivers and other essential elements of our organization.

### Industry, scientific and regulatory overview

Overview of vaccines and antibodies	Vaccines and antibodies are the biopharmaceutical areas in which we are predominantly active.
Regulations applicable to the biopharmaceutical industry	Overview of the general regulatory environment of biopharmaceuticals, including market-authorization and pre-qualification.

### Business drivers

Strong R&D pipeline	We believe that each of our pipeline products targets unmet medical needs, improves current medication or is otherwise marketable due to predictive study models and/ or favorable regulatory conditions.
Licensing our cutting-edge technologies	We developed an array of excellent technologies with applicability to vaccines, therapeutic proteins and gene therapy.
Broad range of vaccine products	We produce and sell established paediatric, travel and respiratory vaccines against a broad range of infectious diseases, focusing strongly – but not exclusively – on unmet medical needs in developing countries.

### Additional information on the Company

Partners, agreements, investments and other collaborations	An overview of our partners, agreements, investments and other collaborations relevant to our operations.
Intellectual property	Our success and ability to compete depends in large part on registration of our proprietary technology.
Other information	Other information on topics relevant to the organization, which include legal proceedings, property, plant and equipment, insurance, supply of materials, employees and dividend policy.

### Industry, scientific and regulatory overview

The biotechnology field is one of rapid change and innovation. We expect that this industry will continue to experience significant technological changes in the years ahead. We operate in highly competitive markets and experience competition from companies that have similar or other technologies, and other products or forms of treatment for the diseases we target. As these companies develop their technologies, they may develop proprietary positions in the areas of our core technologies or obtain regulatory approval for alternative technologies or commercial products.

### Overview of vaccines

#### General

Vaccines are designed to protect people against potentially life-threatening diseases. They are biological substances that stimulate an immune response that allows a vaccinated individual to resist future infections and disease. The immune system recognizes vaccine agents as foreign, destroys them, and ‘remembers’ them. When the virulent version of an agent comes along the body recognizes the protein coat on the virus, and thus is prepared to respond by neutralizing the target agent before it can enter cells, and by recognizing and destroying infected cells before that agent can multiply to vast numbers.

Vaccines have contributed to the eradication of smallpox, one of the most contagious and deadly diseases known to man. Other diseases such as rubella, polio, measles, mumps, chickenpox, and typhoid are nowhere near as common as they were a hundred years ago. As long as the vast majority of people are vaccinated, it is much more difficult for an outbreak of disease to occur or to spread. Significant developments include the introduction of combination vaccines and the development of new vaccine technologies that may advance vaccine development.

A variety of vaccine formats are in use today and others are evolving through ongoing research and development efforts. Some of the most common vaccine formats include live-attenuated virus vaccines, inactivated whole-killed virus vaccines, sub-unit vaccines, DNA vaccines, recombinant vector-based vaccines, synthetic vaccines and peptide-based vaccines.

A large variety of vaccine technologies are under development in an attempt to improve safety and overall vaccine efficacy. The key objectives of current vaccine technology research and development are to make safer vaccines without compromising efficacy, to generate new vaccines with stronger and broader immunogenicity, to make vaccines using more efficient manufacturing processes and to make vaccines easier to administer.

### **Market and competition**

According to the “Global Vaccine Market Forecast to 2012” published by RNCOS, the compound annual growth for the global vaccine market will be over 13% and the global vaccine market is expected to reach \$ 34.0 billion by 2012. Vaccines, which were earlier thought as a low margin, low growth industry, have emerged as one of the most lucrative segments in the pharmaceutical industry. The competitive landscape of the global vaccine market shows a highly concentrated structure, with the top four players accounting for around 74% of the total market in 2008.

Segment-wise, paediatric vaccines presently dominate the global vaccine market but adult vaccine segments could define the future direction of growth. The cancer vaccine market is presently one of the most lucrative areas for vaccine manufacturers. Flu vaccines have huge demand at present and all major vaccine manufacturers are seeking to develop their own flu vaccines. Owing to lower margins and the mature nature of these markets, the basic and enhanced paediatric markets are expected to show stagnant growth in

the future. On the other hand, launch of a number of new vaccines will make the addiction, cancer and proprietary paediatrics/adolescent vaccine market highly dynamic.

Other biotechnology and pharmaceutical companies that are focused on developing vaccines against infectious diseases include Wyeth, sanofi pasteur, Merck & Co., GlaxoSmithKline, Novartis, Acambis, Baxter, GenVec, Bavarian Nordic, Baxter, Solvay, Vical and Amgen.

With respect to vaccines developed on Per.C6 technology, other companies use alternative non-human expression platform technologies. There are also other human expression technologies for licensed and marketed vaccines, as well as human cell lines supporting products in development.

### **Overview of antibodies**

#### **General**

Antibodies are proteins made naturally by cells of the body's immune system. They function as one of the body's principal defense mechanisms against pathogens, which are disease causing agents such as parasites, viruses or bacteria. Antibodies recognize and bind to invading pathogens, ultimately eliminating them, thus playing a crucial role in protecting humans against disease. Because of their binding characteristics, antibodies can distinguish subtle cell differences between healthy and diseased cells. Antibodies are used to develop therapeutic products that can

- Bind to and block a key interaction of a disease-related cell, such as an inflammatory cell;
- Block infectious agents; and
- Trigger the death of a target cell, such as a cancer cell.

Antibodies may also be used to bind and neutralize toxic products, to develop diagnostic products to detect viruses or bacteria and as tools in scientific research such as genomics and proteomics.

Methods for generating monoclonal antibodies have evolved considerably over the last 25 years. The technology originally involved immunizing mice with a target molecule and isolating relevant antibody-producing cells from the mice. Because monoclonal antibodies of rodent origin are recognized as foreign proteins and are rapidly eliminated when applied in humans, methods were developed to produce therapeutic antibodies that are of human origin. These antibodies can be developed either using transgenic

## Information on the Company continued

mice or by means of phage antibody-display technology. Transgenic mice are genetically engineered mice that carry human antibody genes. This allows the immune systems of mice to generate human monoclonal antibodies in response to any administered antigenic material. Phage antibody-display technology allows human antibody genes to be cloned into bacteriophages, which are viruses that only infect bacteria. Phages displaying antibody fragments that attach to specific molecules can be selected, enabling isolation of antibodies against targets and/or enabling the identification of target molecules. Phage antibody-display libraries are large collections of antibody-phages for use in identifying the targets and related antibodies.

### *Market and competition*

Following the success of recombinant proteins, therapeutic monoclonal antibodies represent the second wave of innovation in the biotechnology industry during the past twenty years. In 2009, market researcher Datamonitor forecasts a six year compound annual growth rate of 10.3 per cent over the period 2008-14 for monoclonal antibodies to approach \$ 60 billion sales by 2014.

Approximately thirty therapeutic monoclonal antibodies have been approved around the world. A number of these drugs have attained blockbuster status, with sales reaching the coveted \$ 1 billion mark and beyond. Several products generated sales of over \$ 4 billion each in 2008, and global sales for this entire sector surpassed \$ 30 billion in 2008.

Other biotechnology companies, including UCB Celltech, Genentech and PDL BioPharma, currently generate humanized antibodies, and Cenacor, Biogen IDEC, Medarex, Inc., GenMab, and Regeneron produce human monoclonal antibodies from transgenic mice. Abbott, MedImmune, MorphoSys AG and Dyax generate fully-human monoclonal antibodies using phage antibody-display libraries that are similar to ours. Companies such as XOMA and SCA Ventures, Inc., a subsidiary of Enzon Corporation, are also working in the field of phage display libraries and related technologies.

In the area of infectious disease antibodies, potential competitors include serum antibody companies such as CSL and Baxter, and monoclonal antibody companies like MedImmune.

### **Regulations applicable to the biopharmaceutical industry**

We operate in a highly regulated industry. Our products require approval of government health authorities before they can be sold, and require significant pre-clinical and clinical testing before approval will be granted. Our research and development and production activities involve the use of hazardous materials, including biological materials, many of which we need special approval to obtain and all of which are subject to regulation regarding their handling and disposal. Environmental laws and regulations and laws and regulations relating to safe working conditions, laboratory conditions, and laboratory and manufacturing practices also apply to our operations. We conduct our operations in a manner designed to comply with applicable regulations and we believe that we have all the licenses and permits required to carry out our current activities. In most countries, it is necessary to obtain mandatory approval to market a pharmaceutical or medical product. The granting of such approval is subject to a detailed evaluation of data submitted by the applicant related to the quality, safety and efficacy of the product.

Obtaining product approval is a costly and time-consuming process. Any products our licensees or we develop will require regulatory clearances prior to clinical trials and additional regulatory clearances prior to being produced and distributed commercially. These regulatory processes are generally stringent and time consuming. We expect the European Medicines Agency (EMA) in the European Union, the FDA in the US, the College ter Beoordeling van Geneesmiddelen (CBG) in the Netherlands and comparable agencies in other countries to subject new biopharmaceutical products to extensive regulation. These regulatory requirements with which we and our licensees will have to

comply will evolve over time due to the novelty of the biopharmaceutical products and therapies currently under development. Fortunately, the harmonization of these requirements is promoted at an international level (International Conferences on Harmonization (ICH)) to avoid unnecessary repetition of studies when seeking approval in various countries. Under the current definitions, we believe that products developed using our technologies will be regulated either as biological products or as drugs.

To obtain regulatory approval from the relevant authorities, pre-clinical and clinical trials must be conducted to demonstrate the safety and efficacy of the product candidates. Clinical trials are the means by which experimental drugs or treatments are tested in human volunteers. New therapies typically advance from laboratory research testing through pre-clinical testing and finally through several phases of clinical human testing. Clinical trials are normally done in the following phases:

- **Phase I:** First clinical trial of a new compound generally performed in a small number of healthy human volunteers, to assess clinical safety, tolerability as well as metabolic and pharmacologic properties.
- **Phase II:** Clinical studies that test the safety and efficacy of the compound in patients with the targeted disease with the goal of determining the appropriate doses for further testing and evaluating study design as well as identifying common side effects and risks.
- **Phase III:** Large-scale clinical studies with several hundred or several thousand patients to establish safety and effectiveness for regulatory approval for indicated uses and to evaluate the overall benefit/risk relationship.
- **Phase IV:** (post commercialization trials) these trials involve the safety surveillance and ongoing technical support after market approval.

Once a product is approved, the manufacturing and marketing of the product remains subject to periodic review. Changes in applicable regulations, breaches of regulatory requirements or the discovery of problems related to the manufacturing, safety, quality or efficacy or stability as well as changes in the characteristic of a product inherent to its biological origin may result in the imposition of restrictions upon the manufacturing and sale of such products, including at worst withdrawal of the product from the market and/or the revocation of the relevant regulatory approvals.

### **Pre-qualification applicable to the biopharmaceutical industry**

National and regional governments rely on the pre-qualification granted to biopharmaceutical products by evaluative bodies such as the WHO and, in some cases, simply elect not to purchase products which have not been granted pre-qualification of approval.

The WHO Pre-qualification is carried out to facilitate access to medicines that meet unified standards of quality, safety and efficacy.

Pre-qualification was originally intended to give United Nations procurement agencies, such as UNICEF, the choice of a range of quality medicines. With time, the growing list of medicines that have been found to meet the set requirements has come to be seen as a tool for anyone purchasing medicines in bulk, including countries themselves and other organizations.

Any manufacturer wishing their medicines to be included in the pre-qualified products list are invited to apply. Each manufacturer must present extensive information on the product (or products) submitted to allow qualified assessment teams to evaluate its quality, safety and efficacy. The manufacturer must also open its manufacturing sites to an inspection team that assesses working procedures for compliance with WHO Good Manufacturing Practices (GMP).

The pre-qualification does not intend to replace national regulatory authorities or national authorization systems for importation of medicines.

### **Business drivers**

#### **Strong R&D pipeline**

Product pipeline programs include vaccines against yellow fever, influenza, tuberculosis, Ebola and Marburg, malaria, HIV, and antibodies against rabies, a broad range of influenza strains and hepatitis C. Our R&D activities are concentrated in our headquarters in the Netherlands, but we also have development facilities in Switzerland and Korea.

## Information on the Company continued

### Overview of our pipeline based on proprietary technologies

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Our PER.C6 technology, complemented by our AdVac and MAbstract technologies, drives the development of our product pipeline for vaccines and monoclonal antibodies. We continue to develop our technologies while selecting product leads for further development based on careful product selection criteria that support our long-term business objectives. We have in the past and may again in the future, enter into collaborative and/or strategic alliance arrangements with third parties to co-develop and market products.

Our primary focus is the development of a range of novel vaccine and antibody products in the area of infectious diseases. We currently have a number of potential products that we are developing using our technologies:

- Our candidate influenza, rabies and hepatitis C human monoclonal antibodies are generated and produced using our PER.C6 and MAbstract technologies;
- An influenza vaccine, in collaboration with sanofi pasteur is being developed using our PER.C6 technology; and
- Our malaria, TB vaccine and Ebola and Marburg candidates are recombinant vaccines based on PER.C6 technology that also employ AdVac technologies.

### Overview of our vaccines in development

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#### Yellow fever vaccine

We developed our yellow fever vaccine, Flavimun, based on a well-established vaccine formerly produced by the Robert Koch institute in Germany. The product was submitted for registration with the Swiss authorities in the first quarter of 2009. A dedicated team is currently reviewing outstanding questions from the Swiss authorities and will respond as soon as possible.

#### Influenza

##### *Epidemic (or seasonal) influenza vaccine*

In December 2003, we entered into a strategic agreement with sanofi pasteur to further develop and commercialize novel influenza vaccines using our PER.C6 technology. A Phase II trial of the cell culture-based seasonal influenza vaccine was initiated in the US and started in the fourth quarter of 2007. In the third quarter 2008, we received a milestone payment for the progress of the Phase II trials involving healthy adult volunteers in the US. The trials focus on the safety profile and immunogenicity of the cell-based vaccine. All data collected so far confirm that the PER.C6 cell line supports the growth of all flu virus strains in high quantities.

##### *PANFLUVAC*

In July 2009, the PANFLUVAC consortium consisting of eight European research partners, including Crucell, completed the first stage of their Phase I clinical trial in healthy volunteers, using a combination of virosome vaccines against A/H5N1 influenza and an Immune Stimulating Complex (ISCOM) adjuvant. The results show that the vaccine is safe and tolerable. Furthermore, the vaccine is very immunogenic and fulfills all serological Committee for Proprietary Medicinal Products (CPMP) requirements for influenza vaccines.

##### *Influenza vaccine production technology*

Influenza vaccines are classically produced on embryonated chicken eggs. Currently, cell culture systems are being developed for more efficient influenza vaccine production based on Madin Darby Canine Kidney (MDCK) cells and VERO cells. In contrast to MDCK and VERO cells, PER.C6 cells grow well in suspension and are thus easily scalable, permitting the production of cost-efficient vaccines in large quantities. PER.C6 cells possess the different receptors required for the production of vaccines against both human and animal strains of influenza that may present a pandemic threat.

## About influenza

Influenza, commonly known as 'flu', affects large sections of the world's population each year. The disease is characterized by annual winter outbreaks, which often reach epidemic proportions due to the fact that the virus can mutate quickly, often producing new strains against which humans do not have immunity. Typical symptoms of flu are usually relatively mild but can become life threatening in vulnerable patient groups, such as the elderly and immunodeficient individuals. In a growing number of countries, small children have been added to the list of preferred protection groups. Transmission of the flu virus occurs through airborne particles and upon infection, the incubation period ranges from one to three days. According to the World Health Organization an estimated 250,000 to 500,000 people die annually from influenza-associated complications.

In addition to these annual epidemics, global pandemics may arise as a consequence of a major genetic shift in the influenza virus leading to a deadly new virus strain to which the human population does not have immunity. The pandemic (H1N1) 2009 influenza virus is an example of a virus that has never circulated among humans before. After outbreaks in North America early in 2009, the virus spread rapidly around the world causing a pandemic. Mitigating its effects is a public health priority. Concerns still exist that a new avian influenza strain (i.e. H5N1 and H9N2) endemic among birds in Asia, and showing high pathogenicity for humans, could present a genuine pandemic threat.

## Tuberculosis

Crucell is developing a recombinant tuberculosis (TB) vaccine based on our AdVac and PER.C6 technology. The development of this vaccine is being carried out in collaboration with the Aeras Global TB Vaccine Foundation (AERAS). The Crucell-Aeras TB vaccine (AERAS-402/Crucell Ad35) program is focusing on an AdVac based vaccine that can boost the immune response against TB, initially induced by Bacille Calmette-Guérin (BCG) vaccine. BCG is currently the only vaccine licensed to help prevent TB.

A first Phase I clinical trial, launched in October 2006 in Kansas, USA, indicated that the vaccine candidate is safe in healthy adults. Results of a second study with the candidate vaccine that was launched in May 2007 showed that both critical arms of the cellular immune system, CD4 and CD8 immune T-cells, were induced and that in those participants who responded, CD8 immune responses were

considerably higher than had ever previously been seen in a TB vaccine study.

Two Phase I studies in healthy adults in St. Louis, Missouri, USA, focusing on the immunogenicity and safety of two boost doses of the candidate vaccine administered at three to six month intervals after BCG priming in healthy adults have been completed. Data from these studies specifically indicate that two injections of the candidate vaccine are immunogenic, with an acceptable safety profile, when used with a BCG prime in combination with the candidate vaccine in BCG vaccinated healthy adults, regardless of the boosting interval. This immune response is greater than that detected in the absence of BCG prime, supporting the possible utility of the candidate vaccine as a booster vaccine. A follow-up study conducted in the USA in healthy adults showed that the candidate vaccine had an acceptable safety profile when an increased dose was administered.

A Phase I clinical trial in Kenya that began in October 2008, to test the safety of the candidate vaccine in BCG-vaccinated adults with or without latent tuberculosis, was completed in 2009. The study was conducted by the KEMRI/ Walter Reed Project-Kisumu at their Kombewa Clinical Trials Center near Kisumu, in Western Kenya. Analysis is ongoing and no safety issues have been identified.

In April 2009, a Phase I clinical trial in infants was started in South Africa. This is the first clinical trial designed to test this candidate vaccine in infants. This Phase I study is being conducted by the South African Tuberculosis Vaccine Initiative (SATVI) in the Western Cape region of South Africa. The main objective of the study is to test the safety of the TB candidate vaccine in infants previously vaccinated with BCG vaccine. This study is fully enrolled and dosing is ongoing in the last cohort. No safety issues have been identified to date.

In January 2010, a Phase I clinical trial was initiated in Portland, Oregon, USA. This trial is using a known immunogenic regimen of BCG and the candidate vaccine in healthy adults, followed by collection of large numbers of immune cells for more detailed analysis of the immune response to the candidate vaccine.

The first Phase II study of the vaccine candidate, started in October 2008, is being conducted by the University of Cape Town Lung Institute, South Africa in conjunction with the South African Tuberculosis Vaccine Initiative. In this dose



## Information on the Company continued

escalation study in adults who have had active TB, no evidence of an unacceptable safety issue has been found in the 72 subjects enrolled to date. Preliminary data indicate that the candidate vaccine induces CD8-cell immune responses in patients who have completed TB treatment.

### About tuberculosis

TB is a major cause of illness and death worldwide, especially in Asia and Africa, with over 9 million new cases diagnosed in 2008. According to the World Health Organization (WHO), an estimated 1.3 million HIV-negative and 0.5 million HIV-positive people died from TB in 2008. One third of the world's population has been infected with the TB bacillus and current treatment takes 6-9 months. The current TB vaccine BCG, developed over 85 years ago, reduces the risk of severe forms of TB in early childhood but is not very effective in preventing pulmonary TB in adolescents and in adults, the populations with the highest TB rates. As the disease is changing and evolving, new vaccines are even more crucial to control any pandemic. TB is the leading cause of death for people living with HIV/AIDS, particularly in Africa. Multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB) are hampering treatment and control efforts. A need for an alternative vaccination approach has emerged in the last two decades.

### Malaria

We are developing a recombinant malaria vaccine based on our AdVac technology and produced on our PER.C6 production technology. The vaccine is made by inserting the gene for the circumsporozoite protein (CSP) from a malaria parasite into an adenoviral vector, which acts as a 'vehicle' for vaccination delivery.

The efficacy of our malaria vaccine candidate was tested in pre-clinical models. Studies in a murine model showed that a single administration of a prototype AdVac vaccine, provided protection against the specific parasite. In partnership with the NIAID, Crucell's malaria vaccine entered a Phase I trial in the US in January 2007. The study is being carried out on two sites, Vanderbilt University in Tennessee and Stanford University in California. All four cohorts have been enrolled

and in December 2009 boost vaccinations for the final group of volunteers were completed. Ongoing safety monitoring has revealed no significant safety concerns to date. Preliminary examination of the blinded data from the first four cohorts indicates that the vaccine is immunogenic. Detailed analysis of the data is ongoing and unblinding is expected in the second quarter of 2010.

In July 2009, Crucell announced a new collaboration with partners in the US-based MVI and USAID MVDP to accelerate development of a promising new type of malaria vaccine. Through funding from the USAID MVDP, the partners will conduct studies to determine the effectiveness of Crucell's novel prime-boost vaccine approach against the malaria parasite *P. falciparum*. This approach uses Crucell's proprietary recombinant adenoviruses (a type of virus associated with the common cold and other mild respiratory infections), to deliver a malaria antigen to the immune system. Using Crucell's AdVac technology with two different adenovirus vectors—Ad35 and Ad26—as delivery mechanisms, this approach seeks to elicit a protective immune response obtained from delivering the CSP.

### About malaria

Malaria is a life-threatening infectious disease caused by the plasmodium parasite and transmitted from person-to-person through the bite of a female *Anopheles* mosquito. It is currently one of the most lethal communicable diseases. The disease currently represents one of the most prevalent infections in tropical and subtropical areas causing severe illness and death worldwide. According to the World Health Organization's latest report, 243 million malaria cases led to nearly 863,000 deaths in 2008. Most of these deaths occur among children and pregnant women in the developing world, especially in sub-Saharan Africa. Unfortunately, mortality associated with severe or complicated malaria still exceeds 10-30%. The widespread occurrence and elevated incidence of malaria are a consequence of discontinued malaria control programs and increasing numbers of drug-resistant parasites and insecticide-resistant parasite vectors. Other factors include environmental and climatic changes, civil disturbances and increased mobility of

populations. Although the overwhelming majority of morbidity and mortality associated with malaria occur in the developing world, this disease also affects travelers.

#### **Multivalent filovirus (Ebola and Marburg) vaccine**

Crucell is developing an Ebola vaccine in collaboration with the Vaccine Research Center (VRC) of the NIAID. The objective of the Collaborative Research and Development Agreement (CRADA) with the VRC is to jointly develop, test and manufacture an adenovirus-based Ebola vaccine. Under the terms of the agreement, we have an option for exclusive worldwide commercialization rights to the Ebola vaccine resulting from this collaboration.

In experiments conducted by the VRC together with the US Army Medical Research Institute of Infectious Diseases (US AMRIID) during the first half of 2004, our vaccine candidate confirmed single-dose protection in pre-clinical testing against Ebola. What set the results of this trial apart from the earlier successful trial, which established a proof-of-concept, was that the vaccine in this instance was produced on PER.C6 technology.

In March 2005, we extended the CRADA with the US NIH and continue to develop this vaccine and will use the Ebola vaccine results in the development of Marburg and Lassa vaccines. In addition, we obtained an exclusive license to certain NIH patents to develop and commercialize recombinant vaccines against Ebola.

In October 2008, we secured a NIAID/ NIH contract aimed at advancing the development of Ebola and Marburg vaccines, ultimately leading to a multivalent filovirus vaccine. The contract provides funding of up to \$ 30 million, with additional options that may be exercised at the discretion of the NIAID for an additional \$ 40 million. The Phase I study of an Ad5 and PER.C6-based Ebola vaccine that Crucell is developing in partnership with the Vaccine Research Center (VRC) of the NIAID/NIH, showed safety and immunogenicity at the doses evaluated. Based on these results, a second Phase I study of an Ebola and/or Marburg vaccine is anticipated. This will use alternative multivalent adenovirus vectors that are able to bypass pre-existing immunity against Ad5.

#### **About Ebola and Marburg**

The Ebola and Marburg viruses are capable of causing hemorrhagic fever, a severe, often-fatal disease in humans characterized by high fever and massive internal bleeding,

causing death in 50% to 80% of all cases. Ebola and Marburg outbreaks occur regularly in tropical Africa, affecting both human and great ape populations. Since the Ebola virus was first recognized, approximately 2,200 cases, including over 1,500 deaths, have been reported. To date, over 440 cases of Marburg have been reported with approximately 360 fatalities. Ebola and Marburg usually appear in sporadic outbreaks, and spread within a health-care setting. Because of the high disease-related mortality rates and lack of any vaccine or therapy, the Ebola and Marburg viruses are on the US Centers for Disease Control and Prevention Category 'A' list of bio terror agents, together with smallpox and anthrax.

#### **HIV**

In August 2005, Crucell, along with Harvard Medical School, was awarded a \$ 19.2 million grant by the US NIH to develop new adenovirus vector-based vaccines against HIV/AIDS. The Investigational New Drug Application (IND) for Phase I of the trial with Harvard Medical School (supported by the NIH) was approved by the FDA in January 2008. In April 2008, the Company announced the start of a Phase I clinical study of the novel HIV recombinant AdVac-based vaccine that Crucell is jointly developing with the Beth Israel Deaconess Medical Center, using adenovirus serotype 26 (rAd26) as vector. The rAd26 vector is specifically designed to avoid the pre-existing immunity to the more commonly used adenovirus serotype 5 (Ad5). The Phase I clinical study is being conducted at the Brigham and Women's Hospital in Boston, Massachusetts, USA and is focused on assessing the safety and immunogenicity of the vaccine. Enrollment is ongoing and involves 48 healthy volunteers. Dose escalation has proceeded without difficulty and the third cohort has been fully enrolled. Boost vaccinations are ongoing. On 21 October 2009 preliminary results of the Phase I study were presented at La Conférence AIDS Vaccine 2009 in Paris, France. The preliminary results of this study show that this HIV candidate vaccine is safe and immunogenic.

#### **About HIV**

Human immunodeficiency virus or HIV is a retrovirus that causes acquired immune deficiency syndrome (AIDS), a condition in humans in which the immune system begins to fail, leading to life-threatening infections. HIV infection occurs on a global scale. A joint United Nations Program on HIV/ AIDS and the WHO estimate that AIDS has killed more than 25 million people since it was first recognized on December 1, 1981, making it one of the most destructive pandemics in human history.

## Information on the Company continued

There currently is no treatment for HIV or AIDS. The only known methods of prevention are based on avoiding exposure to the virus or, failing that, an antiretroviral treatment directly after a highly significant exposure, called post-exposure prophylaxis (PEP). Protective sex is another form of prevention of the deadly disease. Antiretroviral drugs (ARVs) which significantly delay the progression of HIV to AIDS and allow people living with HIV to live relatively normal, healthy lives, have been available in wealthier parts of the world since around 1996.

### Overview of our human monoclonal antibodies in development

#### Rabies human monoclonal antibody combination (CL184)

Although many experimental therapies have been utilized to try to save clinically ill rabies patients, there is no recognized treatment for rabies after symptoms of the disease have appeared. However, an effective rabies vaccine and antibody regimen can provide protection against rabies when administered immediately after an exposure. Post-exposure prophylaxis (PEP) is indicated for persons exposed to an animal proven or suspected to be rabid. PEP should begin as soon as possible after an exposure occurs. There have been almost no PEP failures reported when PEP was given promptly and appropriately after an exposure to rabies. Current PEP therapy for severe exposures (transdermal lesions) consists of administration of human immunoglobulin (HRIG) or equine (ERIG) polyclonal immunoglobulin and rabies vaccine. For reasons of safety and availability, alternative products to HRIG or ERIG are advocated, and the development of rabies virus-specific monoclonal antibodies has been recommended, by the WHO.

Crucell's monoclonal antibody combination against rabies is being developed in close collaboration with sanofi pasteur using Crucell's PER.C6 technology.

This antibody combination is designed to be used in combination with a rabies vaccine for PEP against this fatal disease.

The rabies human monoclonal antibody combination was granted a "Fast Track" designation by the FDA Department of Health and Human Services, ensuring priority handling of the regulatory application. Under the terms of the collaboration agreement with sanofi pasteur, Crucell will be responsible for manufacturing the commercial product and has retained exclusive distribution rights in Europe, co-exclusive distribution rights in China and the rights to sell to supranational organizations such as UNICEF, while sanofi pasteur will have exclusive distribution rights for all other territories and co-exclusive distribution rights in China.

Promising Phase I data in 2007 showed no serious adverse effects and demonstrated the expected rabies neutralizing activity upon administration.

Positive preliminary results of the Phase II US study were presented on October 1, 2008. A second Phase II clinical study evaluating the monoclonal antibody combination together with a rabies vaccine in healthy children and adolescents was conducted in the Philippines from May to October 2008. In June 2009, Crucell announced the results of the Philippines study, which showed that the antibody combination was safe and well tolerated. Neutralizing activity levels in subjects given the antibody product were similar to those in subjects given human immunoglobulin (HRIG), the current standard for inducing immediate, passive immunity. All study participants reached adequate immunity levels. This study in children further broadens the potential patient population for Crucell's rabies monoclonal antibody combination. An additional Phase II clinical study to be conducted in India is scheduled to start in 2010. The rationale for this study is to collect safety and neutralizing activity data of the CL184 antibody in combination with the vaccine in a simulated rabies post-exposure prophylaxis setting to be used in Phase III.

#### About rabies

Rabies is a viral disease of mammals most often transmitted through the bite of an infected animal. The virus infects the central nervous system, causing encephalopathy and ultimately death if medical treatment is not sought before

symptoms become more severe. Rabies is prevalent in all the continental regions of Europe, Asia, America and Africa. Globally, approximately 10 million people a year are treated after exposure to rabies. More than 50,000 people are thought to die of the disease each year, mainly in China and India.

### **Human monoclonal antibodies against a broad range of influenza**

Crucell's scientists discovered a set of human monoclonal antibodies that provides immediate protection and neutralizes the broadest range of H5N1 strains. When tested in pre-clinical models for prevention or treatment of a potentially lethal H5N1 infection, this antibody was shown to prevent death and cure the disease.

In another pre-clinical study, Crucell's mAb CR6261 was compared with the most current anti-influenza drug, oseltamivir, in terms of its value for flu prevention and treatment. In December 2008, Crucell announced that its monoclonal antibody had strongly outperformed oseltamivir in these tests. The flu strains tested included the 'bird flu' strain H5N1, which, experts fear, has the potential to cause a pandemic, and H1N1, which is similar to the strain responsible for the devastating pandemic in 1918. Importantly, the study showed that CR6261 provides immediate protection against the influenza virus, suggesting that it will be able to prevent disease spread. In contrast, oseltamivir was less efficacious and in some cases not effective at all.

The characterization of the antibody was described in the online journal PLoS ONE on December 16, 2008. An imaging study published in the prestigious journal Science on 26 February 2009 described the mechanism that accounts for the broad-spectrum protection afforded by the antibody by showing how it binds to a part of the influenza virus that is less likely to mutate from one viral strain to the next. Antibodies produced by the body in response to influenza infection or vaccination, by contrast, bind to a part of the virus that tends to mutate more frequently, thus limiting the efficacy of human monoclonal antibodies to rapidly mutating influenza viruses.

In August 2009, Crucell received an award from the US National Institute of Allergy and Infectious Diseases (NIAID) and US National Institutes of Health (NIH) for the development of monoclonal antibodies for the treatment of seasonal and pandemic influenza. The award provides funding of up to \$ 40.7 million, with additional options that may be exercised at the discretion of the NIH worth a

further \$ 28.4 million, bringing the potential total award amount to \$ 69.1 million.

In September 2009, JNJ, through its subsidiary Ortho-McNeil-Janssen Pharmaceuticals, Inc., and Crucell entered into a strategic collaboration focusing on the discovery, development and commercialization of monoclonal antibodies and vaccines for the treatment and prevention of influenza and other infectious and non-infectious diseases. The immediate focus of the collaboration will be the development and commercialization of a universal monoclonal antibody product (flu-mAb) for the treatment and prevention of influenza. The focus of the long-term collaboration will be on new discovery programs leading to the development and commercialization of a universal influenza vaccine as well as the development of monoclonal antibodies and/or vaccines directed against up to three other infectious and non-infectious disease targets. See 'Paediatric vaccine – About Influenza' in this section for more details on influenza.

### **Hepatitis C Antibody Combination**

In February 2009 we obtained an exclusive license from Stanford University for the development of a monoclonal antibody combination against the hepatitis C virus (HCV). A large panel of fully human monoclonal antibodies against HCV is being evaluated by us in a proof of concept phase. The monoclonal antibodies have been found to neutralize HCV on a number of genotypes tested and each recognizes a different part of the HCV surface protein.

### **About hepatitis C**

Hepatitis C is a contagious liver disease that results from infection with the hepatitis C virus. It can range in severity from a mild illness lasting a few weeks to a serious, lifelong illness. Hepatitis C is usually spread when blood from a person infected with the hepatitis C virus enters the body of someone who is not infected. Today, most people become infected with the hepatitis C virus by sharing needles or other equipment to inject drugs. Before the widespread screening of the blood supply began hepatitis C was also commonly spread through blood transfusions and organ transplants.

Hepatitis C can be either "acute" or "chronic." Acute hepatitis C virus infection is a short-term illness that occurs within the first 6 months after someone is exposed to the hepatitis C virus. For most people (50-80%), acute infection leads to chronic infection. Chronic hepatitis C is a serious disease which in 10-20% of the cases will result in long-term

## Information on the Company continued

health problems such as liver cancer, or even death. It is estimated that there are more than 170 million chronic carriers of the virus at risk of developing serious liver disease and/or liver cancer. There is no vaccine for hepatitis C. There has been a significant improvement in the treatment of hepatitis C in recent years. The drugs Interferon and Ribavirin can successfully treat hepatitis C in some people, though the success of treatment depends on the genotype and the amount of virus in the blood. These drugs are usually taken for 6 to 12 months and can sometimes have serious side effects.

### **Blood Coagulation Factor V**

Pre-clinical work on this program was not conclusive and has been discontinued.

### **Licensing of cutting-edge technologies**

#### **Licensing our technologies to the market**

We generate a portion of our revenues and other operating income from licensing our proprietary technologies to pharmaceutical and biotechnology companies. Our business development strategy involves contacting prospective licensees and partners and assessing their interest in our technologies and products. If the prospective licensee or partner indicates interest we negotiate a license and/or collaboration agreement pursuant to which we deliver the applicable technology to, or collaborate with, the licensee or partner.

#### **Core proprietary technologies**

Our product portfolio is supported through five core proprietary technology platforms.

### **PER.C6 technology**

#### **Overview**

Our PER.C6 technology provides a manufacturing system that can be used to produce a variety of biopharmaceutical products. Crucell's PER.C6 cell line is derived from a single, human retina-derived cell, which was purposely immortalized using recombinant DNA technology. As a result, PER.C6 cells can replicate indefinitely, allowing them to be cultured in single cell suspension under serum-free conditions in quantities appropriate for large-scale manufacturing.

The technology has been successfully adapted to grow without the need for serum components or materials that allow cell attachment (micro carriers) and demonstrates excellent cell densities in bioreactors. These features are important because they allow us to produce safe biopharmaceutical products in sufficient quantities.

In September 2008, DSM Biologics and Crucell announced that the high-titer-fed batch process developed at the PERCIVIA PER.C6 Development Center (PERCIVIA) joint venture in Boston, Massachusetts, USA was scaled up to 250 liters by DSM Biologics scientists. In June 2008, the Company reported record-breaking protein yields of 27 grams per liter using DSM's innovative XD™ technology.

In January 2009, DSM and Crucell entered into an agreement with Bioceros B.V. based in Utrecht, The Netherlands to join their vendor network. Under the terms of the agreement, Bioceros will be a preapproved cell line generation partner for licensees of the PER.C6 cell line located in the European Union.

In March 2009, DSM and Crucell entered into an agreement with KBI Biopharma Inc. based in Durham, North Carolina, USA, to provide cell line generation services of the PER.C6 cell line for licensees of the technology. KBI Biopharma can provide services during the crucial early phase of development for licensees.

There are four areas in which our PER.C6 technology is currently being applied:

### **Vaccine production**

PER.C6 technology can be used as a production system for developing and manufacturing both classical and recombinant vaccines.

- For classical vaccine production, PER.C6 cells are infected with the virus against which the vaccine is meant to protect. The virus is subsequently multiplied on PER.C6 cells to high virus titer, yielding a potent starting material that can be processed and purified to produce a final formulation of a whole-killed, split or sub-unit vaccine; and
- For recombinant vaccine production, the PER.C6 technology produces delivery agents called adenoviral vectors. These vectors have been made replication incompetent and thus are only capable of delivering into the human body a portion of DNA encoding for a protein from the pathogen against which the vaccine is meant to protect. The DNA inserted into the vector can be derived from a virus, a parasite or even bacteria, providing a versatile vaccine vector platform.

### **Protein production**

PER.C6 technology can be used as a production system for developing and manufacturing both antibodies and other proteins. DNA encoding for a particular protein of interest is inserted into PER.C6 cells. These modified PER.C6 cells will secrete the desired antibody or other protein. We are further developing the application of PER.C6 for protein production at PERCIVIA.

### **Gene therapy**

The primary function of PER.C6 technology in the field of gene therapy is the production of adenoviral vectors a gene delivery mechanism based on a common cold virus that carries therapeutic genes and facilitates the delivery of the gene into the cells. Since the PER.C6 technology is the only available cell line that does not allow any formation of classical replication competent adenoviruses during the production of replication deficient vectors, the cell line may be applied across the entire adenovirus gene therapy field.

### **Functional genomics**

Our PER.C6 technology can be used to produce libraries of adenoviruses into which individual human genes are inserted to study gene function. The adenovirus libraries carry many genes with unknown functions, which can be used to determine the role of individual genes in a disease process. We believe that our PER.C6 technology, therefore, represents a key analytical tool in the discovery of new genes and their role in biological pathways and human disease.

### **Key features and advantages**

We believe that our PER.C6 technology has the following key advantages over alternative manufacturing systems:

- PER.C6 technology potentially offers a system for high yield, large-scale biopharmaceutical product production. PER.C6 technology can be cultured at high densities and engineered to produce large quantities of biopharmaceuticals and may reduce production expense.
- PER.C6 cells can be cultured in a serum-free medium, without micro-carriers, using a variety of scaling systems, including bioreactors. This simplifies the expansion from laboratory- to industrial-scale production, which may lead to the production of cost-efficient biopharmaceuticals in large quantities. The use of a serum-free medium also offers the potential to significantly improve the purification of biopharmaceuticals produced using the PER.C6 technology and may facilitate regulatory approval.
- We have filed a Cell Substrate Biologics Master File (BMF) with the US Food and Drug Administration (FDA) describing the PER.C6 technology, including its establishment, development and potential use in production processes. The FDA will only evaluate the PER.C6 technology in the context of Investigational New Drug (IND) applications. We believe that the information in the BMF will facilitate the FDA's approval of any biopharmaceutical product that we or our licensees produce using the PER.C6 technology.
- The PER.C6 technology can now claim to have achieved a broad endorsement within the industry. For an overview of our most important licensees and partners subsidiaries please see the 'Appendix Overview licensees and partners'.
- We believe that antibody and other protein products based on the human based PER.C6 technology may demonstrate enhanced biological properties, rendering them potentially more efficacious. In addition, PER.C6 technology efficiently supports the growth of certain human viruses for vaccine development.



## Information on the Company continued

### AdVac technology

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#### Overview

Crucell is a key player in the development of adenoviral-based vaccines, resulting in the availability of proprietary AdVac vectors. We have generated a wide variety of research and GMP clinical batches based on AdVac technology for diverse infectious diseases.

AdVac technology is based on vectors constructed from adeno viruses that do not regularly occur in the human population, such as Ad35. The technology supports the practice of inserting DNA coding of pathogen-derived proteins into a vector. AdVac technology may also be used to develop gene therapy products. AdVac vectors are used in combination with our PER.C6 technology. Currently AdVac technology is used by Crucell and its licensees to develop vaccines against malaria, TB, HIV/AIDS, hepatitis C (HCV) and hemorrhagic fevers (Ebola, lassa, Marburg). While no adenovirus-based recombinant vaccines are currently licensed for human use, AdVac-based vaccines for malaria, HIV/AIDS, HCV, hemorrhagic fevers, and TB have been successfully constructed and are currently in clinical trials.

Crucell has generated a series of adenoviruses including Ad35 and derivatives thereof as well as manufacturing platforms for these vectors. The AdVac vectors can be produced to carry genetic information derived from viruses, parasites and bacteria, and thereby have the potential to allow immunization against life-threatening diseases.

Crucell has laboratories to develop purification methods closely resembling an end-stage manufacturing process. With this facility we can manufacture Ad35 vaccine vectors for comprehensive pre-clinical programs. These products can be manufactured using PER.C6 technology under serum-free conditions.

#### Key features and advantages

We believe our AdVac technology has the following key advantages over other commonly used vector systems:

- Vectors used with AdVac technology share the advantages of the commonly used adenoviral vectors such as: scalable production, high yields and the ability to mediate a strong T-cell immune response;
- The AdVac technology can circumvent pre-existing immunity offering accurate dose control of the vaccines; and
- AdVac vectors can be engineered to contain small genetic fragments of different viruses, parasites and bacteria. This makes possible the development of a wide variety of novel vaccines against a broad range of dangerous human pathogens.

### MAbstract technology

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#### Overview

Our MAbstract technology can be applied to the discovery of novel drug targets and the identification of human monoclonal antibodies against those drug targets.

MAbstract technology employs a bacteria-infecting virus called a bacteriophage, or phage, which expresses part of a human antibody on its surface. The technology employs a library of phages that carry many different human antibodies. To identify and subsequently isolate relevant antibodies, the library is put in contact with pathogens, or cells suspected of carrying the drug target, or if the target is already known in advance, the library may be put in contact with the target directly. Subsequently, phage antibodies binding to the diseased cells or the known target are separated from phage antibodies that do not bind at all, or bind to healthy cells added to eliminate irrelevant phage antibodies present in the library. Since irrelevant phage antibodies for the target in question are often present in great abundance, the elimination step aids in enriching the phage-antibody population for potentially relevant, selectively binding phage antibodies.

Once such phage antibodies have been isolated, they can either be used to subsequently identify the target or a specific binding place on the target (referred to as epitope), or be used to subsequently isolate the DNA coding for the binding part of the antibody. This part may genetically be combined with other parts of the antibody that have no binding function but have accessory functions in the human immune system. Thus, different formats of antibodies with different modes of action or functions can be made, but with the same specificity for the target.

We use our MAbstract technology to identify antibodies reactive with whole pathogens, antibodies against protein elements from pathogens or antibodies directed against targets already known to be associated with disease. In addition MAbstract can be used to identify targets or epitopes on disease-causing agents that were previously unknown and may make suitable candidates for antibody-based diagnosis, prevention or therapy of the associated disease.

### **Key features and advantages**

MAbstract employs a human-based antibody-display technology. We believe that MAbstract allows for the discovery of therapeutic antibodies with several potential advantages over current technologies. These advantages include the following:

- MAbstract technology selects antibodies for possible therapeutic use and discovers novel drug targets using whole cells, tissues or infectious agents.
- MAbstract technology does not have inherent limitations on antibody specificity.
- MAbstract technology has been used to isolate antibodies for numerous disease applications. Selected antibody specificities can be directly reformatted into antibodies for production using PER.C6 technology.

## **STAR technology**

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### **Overview**

STAR technology is useful for increasing production of recombinant antibodies and therapeutic proteins on mammalian cell lines. It is a two component system consisting of (a) STAR elements that counteract gene silencing, resulting in increased levels of production and improved stability of recombinant proteins, and (b) STAR-select, a very stringent selection system that is directly coupled to the expression of the gene of interest, resulting

in only a few cell lines that all produce the recombinant protein at high levels.

We acquired STAR technology in 2004 through the purchase of ChromaGenics B.V., a privately held biotechnology company based in Amsterdam. In connection with the purchase, we also entered into a contingent payment agreement with the former shareholders of ChromaGenics that could result in us making additional payments of up to € 7.0 million, based upon our receipt of revenues generated from the STAR technology. In 2007, we paid € 2.0 million to the former shareholders under this agreement. No payments were made in 2009 and 2008.

### **Key features and advantages**

We believe our STAR technology has the following key advantages over other gene expression technologies:

- Established mammalian cell banks for antibody and protein production are the starting point for STAR technology, thus specially engineered mammalian cells are not needed;
- The STAR technology allows for very rapid stable mammalian cell clone generation; and
- The STAR technology typically yields stable mammalian cell clones that produce five- to ten-fold more antibody or other therapeutic proteins compared to cell clones generated without STAR.

## **Virosome technology**

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### **Overview**

One of the challenges in vaccine development is the creation of products that contain defined antigens of high purity that efficiently induce a protective immune response. Many antigen preparations are therefore supplemented with adjuvants to enhance the body's immune response to the specific antigens. The most commonly used and approved adjuvants for human use are aluminum salt derivatives, which are known to cause adverse reactions such as irritation and inflammation at the injection site. Virosome technology is used in the manufacture of several of Crucell's registered products where it has an excellent safety record. Virosomes are a broadly applicable adjuvant and carrier system with prospective applications in areas beyond conventional antigen-based vaccines. Our virosome technology offers a tool for developing novel, predominantly synthetic vaccines applicable to infectious and chronic diseases. These vaccines offer additional benefits because they are effective even in immune-suppressed patients and infants.

## Information on the Company continued

### Key features and advantages

We believe our Virosome technology has the following key advantages over other antigen delivery technologies:

- Virosome technology provides a broadly applicable delivery system for antigens or DNA/RNA encoding specific immune stimulatory proteins;
- Virosome technology enables target-specific delivery of antigens and amplification of the immune response;
- Viroosomes stimulate both arms of the immune system, eliciting both antibody and cellular immune responses, against inserted immune stimulatory proteins derived from human pathogens;
- Viroosomes are completely biodegradable and can exert an immune response via different routes of administration; and

### Other proprietary technologies

In addition to our core proprietary technology platforms the Company employs numerous other technologies. Of these other proprietary technologies we would like to highlight the following two.

### Hansenula polymorpha

#### Overview

The yeast expression technology Hansenula polymorpha provides us with a highly efficient production technology for proteins, which can be used as a basis for developing and manufacturing new vaccines. The yeast Hansenula polymorpha production system provides superior characteristics for a wide range of industrial applications. In particular its lack of pyrogens, pathogens or viral inclusions, its ease of genetic manipulation and its robustness in industrial scale fermentations add to its attractiveness for the synthesis of pharmaceutical compounds. Our registered HBV vaccine Hepavax-Gene is based on recombinant production in this yeast.

### Key features and advantages

We believe our Hansenula polymorpha technology has the following key advantages over other yeast expression technologies:

- Hansenula polymorpha provides an expression system with superior characteristics for the synthesis of pharmaceutical compounds, including vaccines;
- Hansenula polymorpha provides a safe production platform lacking pyrogens, pathogens or viral inclusions; and
- Hansenula polymorpha is easy to manipulate genetically and is robust in industrial scale fermentations.

### Recombinant Cholera Toxin B sub-unit technology

Cholera Toxin B (CTB) sub-unit is a powerful inducer of immunity both systemically and mucosally. Numerous applications have shown that coupling of antigen to CTB increases the immunogenicity of the antigen. In some applications simple co-administration of CTB with the antigen has been shown to be effective. This has been shown both for parenteral as well as mucosal (intranasal) applications.

CTB is an efficient mucosal carrier for induction of peripheral immunological tolerance. Oral ingestion of antigen coupled with CTB suppresses peripheral T-cell reactivity to the coupled antigen. The Group has a GMP manufacturing facility for recombinant CTB. The production system is designed so that CTB is produced completely devoid of the toxins.

### Broad range of vaccine products

#### Overview

Our products are marketed by our own sales force as well as by our distribution partners. Our sales are subject to seasonal variations. This is specifically the case for our influenza vaccines as vaccination programs mainly take place in the second half of the year. In addition, our travel vaccines are also subject to seasonal travel patterns.

## Vaccine markets

Our core product portfolio currently consists of eight marketed vaccines in three areas of the vaccine market: paediatric vaccines, travel and endemic vaccines and respiratory vaccines.

## Paediatric vaccines

Our core paediatric vaccines are:

- Quinvaxem, a fully-liquid vaccine for protection against five childhood diseases;
- Hepavax-Gene, a recombinant hepatitis B vaccine;
- Epaxal Junior, a low dosage aluminum-free hepatitis A vaccine (0.25 ml); and
- MoRu-Viraten, a vaccine against measles and rubella (all age groups).

Quinvaxem combines antigens for protection against five important childhood diseases: diphtheria, tetanus, pertussis (whooping cough), hepatitis B and Haemophilus influenzae type b, one of the leading causes of bacterial meningitis in children. It was the first internationally available fully-liquid vaccine containing all five of the above antigens, offering a major advantage in terms of convenience of use. Quinvaxem was co-developed with Novartis, which provides four of the five components in bulk. The fifth component is our vaccine Hepavax-Gene.

We produce Quinvaxem together with our hepatitis B vaccine Hepavax-Gene in Korea. In October 2008 we announced that an agreement was reached to relocate our Korean production facility from the Shingal site in Yongin City, Korea to the Incheon Free Economic Zone, Korea. Construction activities at the new site started in December 2008 and are progressing well. First test runs are planned for the second quarter of 2010.

Because it has been pre-qualified by the World Health Organization (WHO), Quinvaxem is available for purchase by supranational organizations. Supranational organizations are major customers for combination vaccines, which are used in large vaccination programs around the world. In August 2009 we announced a long-term arrangement with UNICEF to supply up to \$ 300 million worth of Quinvaxem for the period beginning 2010 through 2012. The new arrangement is the largest ever received by Crucell. With only half of the tendered volume for the 2010–2012 period awarded to date.

## Hepavax-Gene

Hepavax-Gene is a recombinant hepatitis B (HBV) vaccine made using Crucell's proprietary Hansenula polymorpha expression system. It is one of the WHO's pre-qualified vaccines for active immunization against HBV. A key competitive advantage for Hepavax-Gene is our stable and efficient production system.

## About hepatitis B

HBV is a viral infection of the liver that causes various complications if left untreated and may even ultimately cause death. Transmission of HBV occurs as a result of the exchange of blood, the exchange of fluids during sexual intercourse or the exchange of bodily fluids between an infected mother and a newborn baby at birth.

## Epaxal Junior

Early in 2008, we launched Epaxal Junior, our **low dosage unique aluminum-free hepatitis A vaccine**. The vaccine induces protective antibody levels within 10 days of primary vaccination and provides seroprotection for at least 20 years following the second (booster) dose. It can be fitted into the regular immunization schedule for babies.

## About hepatitis A

Hepatitis A (HAV) is a highly contagious infection that causes temporary acute inflammation of the liver. It can range in severity from a mild illness lasting a few weeks to a severe illness lasting several months. HAV infection produces a self-limited disease that does not result in chronic infection or chronic liver disease. HAV is generally contracted orally and commonly spreads through improper handling of food, contact with household members, sharing toys at day-care centers or eating raw shellfish taken from polluted waters.

## MoRu-Viraten

MoRu-Viraten is a safe, well-tolerated and effective vaccine for protection against measles and rubella in children, adolescents and adults. The immunogenicity and safety of MoRu-Viraten have been confirmed in clinical trials and extensive post-marketing surveillance. MoRu-Viraten is free of avian proteins and antibiotics, posing no risk to children with allergies to these substances. The vaccine has been marketed since 1986 and is on the WHO list of vaccines for purchase by UN agencies.

## Information on the Company continued

### About measles and rubella

Measles is a highly contagious disease caused by the measles virus. It is spread by droplets or direct contact with nasal or throat secretions of infected persons and less commonly through the air or indirect contact. Measles continues to remain a serious public health concern worldwide with 30-40 million cases occurring annually. It may be ultimately responsible for more child deaths than any other single agent and is a major cause of preventable blindness in the world. Rubella is a moderately contagious disease caused by the rubella virus. Transmission of the virus is via airborne droplets. It has been estimated that over 100,000 cases of congenital rubella syndrome (CRS) occur in developing countries each year.

### Travel and endemic vaccines

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Our core travel and endemic vaccines are:

- Epaxal, an aluminum-free hepatitis A vaccine (0.50 ml);
- Vivotif, an oral typhoid vaccine; and
- Dukoral, an internationally licensed oral vaccine against cholera (and ETEC).

Travel vaccines include all vaccine products that protect against diseases that are not native to the region travelers are from, but are present in the regions to which they travel. Generally, the target population groups for these vaccine products are individuals traveling to endemic and epidemic regions. Our vaccines for hepatitis A, typhoid and cholera are classified as travel vaccines.

Our travel vaccines are also increasingly used in expanded immunization programs. Vaccines used in countries with medium to high endemicity could also be characterized as routine or paediatric vaccination. Furthermore, even in some European countries where endemicity is low, childhood vaccination against hepatitis A virus (HAV) is recommended. This vaccine represents a large potential upside for vaccine manufacturers as they can be targeted at multiple markets.

### Epaxal

Epaxal is an aluminum-free and fully biodegradable HAV vaccine, offering significant advantages in terms of tolerability. It was the first product to be based on the virosome technology developed and patented by Crucell. It induces protective antibody levels within 10 days of primary vaccination, and provides seroprotection for at least 20 years following the second (booster) dose. In most countries, the vaccine is licensed for adults and children over the age of one. It is currently licensed in more than 40 countries under the brands Epaxal, HAVpur and VIROHEP-A. See 'Paediatric vaccine – About Hepatitis A' in this section for more details on Hepatitis A.

### Vivotif

Vivotif is a live attenuated typhoid fever vaccine for oral administration. The vaccine is indicated for adults and children over the age of five and has an excellent track record for safety, having been on the market for more than 20 years. Protective efficacy is proven in several large-scale field trials including more than 500,000 subjects. Vivotif is currently licensed in over 30 countries, including the United States. Data suggests that Vivotif may be unique in also protecting against paratyphoid A and B fever which is caused by Salmonella strains similar to Salmonella Typhi.

### About typhoid fever

Typhoid fever is a debilitating and life-threatening illness caused by the bacteria Salmonella Typhi. Symptoms of the disease include fever, weight loss, stomach pain, loss of appetite, delirium, severe diarrhea (in children), constipation (in adults), cerebral dysfunction and intestinal perforation. The disease is transmitted by faecal contamination of food or water, or by person to person contact.

Typhoid fever is endemic in many parts of Africa, Asia and Latin America. 21 million people are estimated to develop typhoid fever each year. 1-4% of persons with typhoid fever die. At least 5 million people are believed to develop paratyphoid fever annually.

## Dukoral

Dukoral is an oral vaccine that protects against cholera and the enterotoxigenic *Escherichia coli* (ETEC) and is registered in more than 60 countries. The vaccine has demonstrated a protective efficacy against cholera of approximately 85% and 60% against ETEC. Dukoral acts by inducing antibodies against both the bacterial components and cholera toxin (CTB). The vaccine is suitable for travelers and is indicated for use in adults and children over two years of age. Pregnant and lactating women may use it.

## About Cholera

Cholera is an acute, diarrheal illness caused by infection of the intestine with the bacterium *Vibrio cholerae*. Over 90% of all cholera cases are mild to moderate and present themselves as ordinary traveler's diarrhea. Approximately 10% of infections develop into severe illness, characterized by profuse watery diarrhea, leg cramps and vomiting, resulting in rapid loss of body fluids leading to shock and dehydration. Without treatment, death can occur within hours. According to the US Center for Disease Control and Prevention, cholera has been very rare in industrialized nations for the last 100 years; however, the disease is still common in other parts of the world and the cholera bacteria can be found in many travel destinations, for example in most part of Asia, Africa and South America. It spreads via contaminated food and water.

## Respiratory vaccines

Our core respiratory vaccine is Inflexal V, a virosome adjuvanted influenza (all age groups).

### Inflexal V

Inflexal V is a virosome adjuvanted Influenza vaccine (subunit), based upon the virosome technology developed and patented by the Crucell company, Bernal Biotech AG. It is the only adjuvanted flu vaccine licensed for all age groups (from 6 months and up). The vaccine's antigen composition follows yearly WHO recommendations. Inflexal V was originally introduced in 1997, is registered in 38 countries and has extensive market experience, with more than 41 million doses confirming its safety profile. The tolerability of Inflexal V is excellent due to its biocompatibility and purity. We refer to the 'R&D pipeline – About influenza' for more information on influenza.

## Additional information on the Company

### Partners, agreements, investments and other collaborations

In addition to our own research and development activities, Crucell collaborates with several leading companies. Through these agreements, our technologies are playing a vital role in the development of a number of vaccine and antibody products.

### Johnson & Johnson

We signed a strategic agreement with affiliates of JNJ in September 2009. This partnership will enable us to accelerate and expand our research and development (R&D) programs and facilitate our move into new markets for our existing products, without compromising Crucell's independence and autonomy. The partnership with JNJ is a strong endorsement of Crucell's in-house capabilities for medical innovation and discovery, and a boost for these capabilities.

As part of this strategic agreement, we issued 14,626,984 shares to JHC Nederland B.V., an affiliate of JNJ, at a price of € 20.63 totaling an amount of € 301.8 million. This represents 18% of our outstanding share capital after issuance. We also entered into a strategic collaboration for the development and commercialization of a universal monoclonal antibody product (flu-mAb) for the treatment and prevention of influenza. In addition, the strategic collaboration involves three innovative discovery programs focusing on the development and commercialization of a universal influenza vaccine as well as vaccines directed against three other infectious and non-infectious disease targets.

### Merck

Since 2000, Crucell and Merck have developed a close working partnership, entering into a number of agreements. In June 2003, Merck and Crucell expanded an existing cooperation agreement and agreed to work closely on matters related to maintenance of the PER.C6 Cell Substrate BMF. We further expanded the relationship in December 2006, when we signed a cross-licensing agreement for vaccine production technology. The agreement allows Merck to use our technology on an exclusive basis in additional undisclosed vaccine fields. In return, we received access to



## Information on the Company continued

Merck's large scale manufacturing technology for our AdVac-based vaccines under development. In September 2007, Merck exercised an option for the exclusive use of our PER.C6 technology and access to our AdVac vaccine technology in two infectious disease areas.

### DSM Biologics

In December 2002, we formed an alliance with DSM Biologics to license our PER.C6 technology as a production platform for monoclonal antibodies and recombinant proteins. The combination of the PER.C6 technology and DSM's manufacturing services provides companies with a turn-key biologic manufacturing solution reducing cost, risk and time to market. Furthering this commitment to the PER.C6 technology, Crucell and DSM established PERCIVIA in August 2006. The innovations resulting from this partnership will be available to PER.C6 licensees to further enhance their development capabilities.

### Sanofi pasteur

We have a strategic agreement with sanofi pasteur since 2003 to further develop and commercialize novel influenza vaccine products based on our PER.C6 technology. The agreement covers both seasonal and pandemic influenza vaccines. Sanofi pasteur has the worldwide rights to develop, manufacture and commercialize PER.C6-based influenza vaccines. Crucell has the commercial rights for Japan.

In December 2007, we signed an exclusive collaboration and commercialization agreement with sanofi pasteur for our rabies monoclonal antibodies to be used in association with rabies vaccine for post-exposure prophylaxis.

### Novartis

Our largest selling vaccine is Quinvaxem. The vaccine is produced by Crucell's subsidiary in Korea and was co-developed with Novartis (formerly Chiron), which provides four of the five vaccine components in bulk. We have a profit-sharing agreement with Novartis for this product.

### Wyeth

In March 2008, we entered into an exclusive agreement with Wyeth pursuant to which we perform contract manufacturing for Wyeth at our Swiss facilities. We will develop and manufacture certain vaccine components that Wyeth will use in clinical studies. These activities take place in our facilities in Bern, Switzerland. Wyeth is responsible for the overall clinical development of the vaccine.

On January 7, 2009, we announced that we were in friendly discussions with Wyeth regarding a potential combination of the two companies. On January 26, 2009, we announced that Wyeth withdrew from these discussions.

### Other collaborations and agreements

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#### Manufacturing service arrangements

We have signed manufacturing service agreements with a number of our licensees and partners. Under these agreements, we have produced and may produce in the future clinical batches of adenoviral materials, antibodies, or other materials using our PER.C6 technology for the applicable licensee. We have received and may receive in the future initial fees upon signing and subsequent payments upon delivery of the batches we produce in accordance with the terms of the agreement.

#### University collaborations

We collaborate with a number of universities worldwide in the areas of vaccines, antibodies, cell lines, gene therapy, cancer and cardiovascular disease. Some of our collaborations provide for royalty payments to be made to the universities in the event product sales arise out of the collaborations. Generally, these collaboration agreements specify that Crucell provides the applicable university with a specific amount of funding and the Group receives certain intellectual property rights and access to the results of the university research.

#### Overview licensees and partners

For an overview of our most important licensees and partners subsidiaries please see the 'Appendix overview licensees and partners'.

## Our equity investments

### Subsidiaries

The following transaction changed the scope of consolidation in 2009:

On June 5, 2009 the Group established Crucell UK Ltd. On July 15, 2009 the Group purchased, via its subsidiary Crucell UK Ltd. selected assets and liabilities of UK-Based Masta for an amount of £ 105. The relevant assets acquired pertain to the customer base and the workforce of the UK fields activities of Masta Ltd. In addition, Masta Ltd received monthly payments from March 1, 2009 to July 1, 2009 for a total amount of £ 304 from the Group as consideration for pre-acquisition costs directly related to the business combination.

The Group recognized the identifiable assets acquired and liabilities assumed at their respective fair values. The consideration allocated to the acquired customer contracts amounted to £ 405. No goodwill was recognized in the business combination.

The following transactions changed the scope of consolidation in 2008:

- In December 2008 SBL Vaccin Holding AB and Vitec AB Rhein Vaccines B.V. legally merged into SBL Vaccin AB; and
- In November 2008 we sold our fully-owned subsidiary Etna Biotech Srl (Catania, Italy) to Zydus Cadila (Ahmedabad, India).

For a complete overview of our most significant subsidiaries please see note 1.1 'Corporate information – List of consolidated companies' in the financial statements.

We are not aware of any legal or economic restrictions on the ability of our subsidiaries to transfer funds to the Company in the form of cash dividends, loans or advances other than withholding taxes due in certain countries in which we operate.

### Associates and joint ventures

At December 31, 2009, we had one associate, ADImmune Corp and one joint venture partner, Percivia. The results of investments in these non-consolidated companies are accounted for under the equity method and amount to a total gain in 2009 of € 2,147 (2008: loss of € 128)

On July 3, 2008 the Group sold all of the 2,625,000 shares it owned in Kenta Biotech AG to Inagro Finanz AG. Prior to this sale, our ownership interest had already been diluted from 37% in 2006 to 22% by the end of 2007. We realized an accounting gain of € 1.6 million on the sale in 2008.

For a complete overview of our associates and joint ventures including results please see '5.9 Investments in associates and joint ventures' in the financial statements.

### Other equity investments

Galapagos N.V. (Galapagos) is a discovery company focused on the rapid identification of disease modifying drug targets through the functional screening of human disease models, and the subsequent progression of these targets into drug discovery. The company is listed on the NYSE Euronext Brussels and NYSE Euronext Amsterdam stock exchanges (ticker symbol: GLPG).

Galapagos holds a royalty free exclusive license to use our PER.C6 technology for conducting activities in the field of functional genomics research. Under the license, Galapagos uses PER.C6 technology in conjunction with Tibotec's bioinformatics technology to generate adenoviral gene libraries. We have agreed with Tibotec to not compete with the activities of Galapagos, which holds the rights to the products and technologies that it develops. The Group owns 5.2% of Galapagos as of December 31, 2009 (2008: 5.8%).

## Information on the Company continued

### Marketing & sales partners

We have established a global marketing & sales infrastructure in our markets in the Benelux, Switzerland, Italy, Spain, Scandinavia, the UK, the US, Canada, Argentina, China, Korea, Indonesia and Vietnam. This sales and marketing infrastructure includes a dedicated sales force for supranational organizations. We have also established a strong network of partnerships to ensure broader market access for our products. The most significant collaborations are:

Our partners:	Marketing, sales and distribution partner for:
Zuellig	several vaccines in China.
Baxter International Inc.	several vaccines in Austria, Germany, Greece and Russia.
Infectopharm Germany	our flu vaccine in Germany.
Novartis	our travel vaccines in France and Germany.
Sanofi pasteur	Dukoral in Canada, Australia and a number of other countries outside Europe and the US.
Sanofi pasteur – MSD	our flu vaccine in the UK (until 2010).
Kedrion	our flu vaccine in Italy.

In September 2009 we launched our own dedicated marketing & sales organization in the United Kingdom by acquiring an experienced team, to strengthen our vaccine sales position in one of the largest travel vaccine markets in Europe. Previously we distributed our travel vaccines through the UK-based company Masta Ltd, and influenza vaccines through Sanofi Pasteur MSD. Our UK marketing & sales organization will market and sell Epaxal, Vivotif, Dukoral and also Inflexal. The distribution of the travel vaccines started in the fourth quarter of 2009. The distribution of the influenza vaccines will start in 2010.

We also distribute and market other companies' products, to strengthen our presence in vaccine or therapeutic protein markets. The most significant collaborations are:

Our partners:	Marketing, sales and distribution partner for:
Sanofi pasteur – MSD	part of the sanofi pasteur – MSD portfolio in Sweden.
Novartis Vaccines and Diagnostics	part of the Novartis vaccine portfolio in Sweden.
Statens Serum Institute Denmark (SSI)	part of SSI's product portfolio in Spain and Sweden.
Green Cross Corporation Korea	Green Cross Corporation's Japanese encephalitis vaccine in Europe.
Netherlands Vaccine Institute (NVI)	part of NVI's product portfolio in the Benelux
Talecris Biotherapeutics	Talecris's product Prolastin in nine Western European countries.

## Intellectual property

Our success and ability to compete depends in large part on our ability to protect our proprietary technology and information, and to operate without infringing on the intellectual property rights of others. We rely on a combination of patent, trademark and trade secret laws, as well as confidentiality, assignment and licensing agreements, to establish and protect our proprietary and intellectual property rights. Our policy is to actively seek patent protection of our intellectual property in the US and Europe, as well as in other jurisdictions as appropriate.

We engage European and Dutch patent attorneys that file, prosecute, defend and enforce patent rights as well as manage our patent portfolio. Our patent portfolio comprised 1,901 active cases (i.e. granted patents in force or pending patent applications) as of December 31, 2009. We aggressively protect our inventions and employ a proactive filing strategy with respect to patent applications. Our portfolio management involves active commercialization and enforcement strategies combined with disposal of cases that we no longer consider commercially attractive.

The following table reflects the total number of active cases (pending or granted) through December 31, 2009, organized according to our different fields of operation. All figures include acquired and jointly owned patent cases, but exclude patent positions licensed-in from third parties.

	Pending	Granted	Active
Vaccines <sup>1</sup>	324	628	952
Antibodies <sup>2</sup>	217	84	301
Technology <sup>3</sup>	186	363	549
Gene Therapy	33	66	99
<b>Total</b>	<b>760</b>	<b>1,141</b>	<b>1,901</b>

<sup>1</sup> Vaccines patent filings relate to AdVac-based, live viral vector vaccines based on our proprietary measles technology, our virosome technology and classical whole inactivated virus, split and sub-unit vaccines.

<sup>2</sup> Antibodies patent filings relate to antibodies and/or drug targets, excluding the enabling technologies that are classified as technology.

<sup>3</sup> Technology patent filings primarily relate to cell-based production technology, adenoviral vector technology, STAR-technology and related technology, functional genomics and target and antibody discovery technology.

### Patent filings

In 2009, we filed patent applications for five new inventions, in the fields of vaccines, antibodies and technology. Our new filings in the vaccine field in 2009 reflect our efforts to further strengthen our patent portfolio in support of product development programs in that area. The new filings in the technology area relate to our continuing effort to

protect and commercialize the PER.C6 technology and related uses of the PER.C6 cell lines, as well as our AdVac technology. Since we are not actively involved in gene therapy research and development, no new filings were made in that area during 2009.

We maintain a geographically diversified filing strategy, depending on our technological and business needs, as well as our view on long-term economic trends and developments in legal systems in various parts of the world. As of December 31, 2009, we had 73 pending applications in the EU<sup>1</sup>, 115 pending applications in the US<sup>2</sup>, 7 international patent applications (so called Patent Cooperation Treaty (PCT) applications<sup>3</sup>) and 565 applications in the rest of the world<sup>4</sup>.

A significant number of our pending patent applications are filed under the PCT, which offers a cost-effective method to seek provisional worldwide protection in more than 100 countries and territories for 30 or 31 months from the filing date. The decision to divide the PCT application into territories in which a granted patent is desired may be postponed until the obtainable scope of protection and the technical and commercial usefulness of the invention becomes clearer. During the pendency of a European patent application, a single application may designate 35 countries but is counted as one pending application. As soon as the European patent application is granted it may be validated for each of the designated countries by filing a translation into the official language of that designated state. Once such a translation has been filed, we count each such patent as a separate patent.

### Patents

At December 31, 2009, we owned or co-owned 66 granted patents in the European Union (EU) territory, 111 patents in the US and 964 patents in the rest of the world.

<sup>1</sup> EU refers to filings made under the European Patent Convention. The EU figures do not include European patent applications designated in PCT applications while still in the international phase.

<sup>2</sup> US figures do not include US patent applications designated in PCT applications while still in the international phase.

<sup>3</sup> Figures reflect PCT applications still in the international phase. Our PCT applications routinely designate all territories and contracting states that are party to the PCT per the international filing date.

<sup>4</sup> Rest of world consists of Australia, Brazil, Canada, China, India, Israel, Japan, Hong Kong, Mexico, New Zealand, Norway, Russia, Singapore, South Africa and South Korea. Rest of world figures do not include PCT applications designating these countries while still in the international phase.

## Information on the Company continued

The following is a summary of the intellectual property rights related to our major products and product developments.

### **Epaxal and Inflexal V**

Epaxal and Inflexal V are the two virosome products which are protected by the patent family 'Immunostimulating and immunopotentiating reconstituted influenza virosomes and vaccines containing them', which will expire in 2012. In addition, the hepatitis A strain used to produce Epaxal is claimed in a patent family which will expire in 2012.

### **Other products**

We have no patent protection for the active substances of Quinvaxem, Hepavax-Gene, Vivotif, Dukoral and MoRu-Viraten.

We seek patent protection, whenever possible, commercially feasible and appropriate, in respect of any technology or product development that is important to our business. Together with our affiliates in Switzerland, Sweden, Italy and Korea, we have several platform technologies and consequently our intellectual property (IP) activities concentrate on protecting these technologies and any improvements thereof in the main worldwide vaccine markets of Europe, the US, Canada, Japan and Australia. However, because some vaccine markets are outside these countries, we have also sought protection in other countries, such as Korea, India and China. The IP portfolio is constantly reviewed to decide on maintenance of individual patents or patent families considering parameters such as actual product performance, product development, patent term, options for commercialization or out-licensing of non-core IP. Our IP tasks are coordinated and patents are filed on a worldwide basis by specialized patent attorneys.

### **Patent enforcement and proceedings**

We may need to litigate or institute administrative proceedings such as oppositions to a patent to enforce or uphold our intellectual property rights or determine the validity and scope of the proprietary rights of others. Likewise, from time to time it may be necessary to defend

our patents in litigation or administrative patent proceedings such as opposition proceedings. We believe that litigation can play a significant role in defining and protecting our intellectual property rights. We are aware, however, that legal and administrative proceedings can be costly and time-consuming, and result in a diversion of resources. As an alternative to litigation, we may enter into licensing, including cross-licensing, arrangements as a means of clarifying the status of our intellectual property rights.

### **Oppositions against patents of the Group**

The basic PER.C6 patent of Crucell is currently in opposition-appeal proceedings, with Crucell as the only appellant and CEVEC Pharmaceuticals, former opponent, as party as of right. In the absence of a cross-appeal by the former opponent, the outcome of appeal proceedings can not lead to a narrower patent than as upheld during first instance proceedings.

In addition to protecting our intellectual property rights, our commercial success also depends on our ability to operate without infringing the intellectual property rights of others. We monitor patent applications to the extent available, patents issued and publications of discoveries in scientific or patent literature to keep abreast of the activities of others in our field and, with the assistance of our internal and external patent counsel and other external advisors, assess whether our activities or products infringe the patents or proprietary rights of third parties. A number of third parties have been granted patents that cover technologies related to ours and similar patents may be granted in the future. We believe that our current activities do not infringe any valid claims of patents or any other proprietary rights of third parties. We will consider the intellectual property rights of others as we continue to identify and develop potential products and may have to enter into licensing or other agreements or use alternative technologies.

### **Oppositions against patents of competitors**

In 2005, we filed opposition against a European patent held by Novartis Vaccines and Diagnostics (formerly: Chiron) related to certain aspects of the production of influenza

viruses in cell culture. The patent was revoked during oral proceedings. An appeal is currently pending. Should the outcome of the appeal be such that the patent is fully re-instated, this may adversely affect the development and the commercialization by Crucell or its licensee of a cell based flu vaccine.

In addition, production of Quinvaxem requires a particular vaccine component that may become the subject of a patent dispute between either GSK and us or GSK and our supplier of that component. The patent on that particular component, held by GSK, could lead to infringement proceedings between GSK and us or GSK and our supplier, although we believe that neither we nor our supplier would be held to have infringed or be infringing that patent. The outcome of legal disputes is invariably difficult to predict with accuracy, but in the event GSK were to prevail in infringement proceedings against us, this would adversely affect our business.

### Technology licenses from third parties

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We licensed numerous technology and patents for specific use as part of our technology platforms from a number of third parties.

We entered into a technology license agreement with Xoma in the field of bacterial expression technology. This license allows us to develop diagnostic and therapeutic antibodies in the field of infectious disease using phage-display technology. The agreement provides us with options to expand the license to cover additional disease fields. Under the terms of the agreement, we pay Xoma milestone payments and royalties on products as and when developed and marketed using the licensed technology.

We also hold a license under the phage antibody display patent portfolio owned or controlled by MedImmune (formerly Cambridge Antibody Technology) and MRC, a cross-license with Transgene S.A. under which we granted to Transgene a non-exclusive PER.C6 license for the manufacture and sale of certain types of vectors for use in gene therapy, and a license for phage antibody-display technology and part human, or chimeric, binding proteins and molecules from Enzon Corporation's subsidiary, SCA Ventures, Inc.

In the field of vaccines, we have concluded an agreement with the Rockefeller University in New York, US. According to

the agreement, we have the exclusive rights to use and exploit the Rockefeller patents related to ex vivo and in vivo targeting of dendritic cells with the use of viral vectors.

The Group has licensed adjuvation technology called ISCOMS from Isconova AB for the development, manufacturing and commercialization of improved influenza vaccines.

In 2009, we entered into a license agreement with Massachusetts General Hospital Corp. (Mass General) for the use of certain gene expression technology owned by that company. Under the agreement, Mass General is eligible to receive a royalty on net sales by Crucell of product manufactured under the license.

In 2009, we acquired the patent portfolio of former Introgen Therapeutics related to adenovirus manufacturing, downstream processing and formulation. Under the agreement, the estate of Introgen Therapeutics is eligible to receive a royalty if we license the acquired patent assets to an unaffiliated third party.

### Technology licenses to third parties

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We have issued certain licenses on an exclusive basis. These licenses generally state that we will not provide the licensed technology to a party other than the exclusive licensee for use in the area covered by the exclusive license. These licenses also generally provide for higher payments than non-exclusive licenses.

When licensing our technology to third parties we seek to obtain access to any improvement patents by our licensees via so-called grant-back provisions to reduce the risk of being exempted from using such improvements for our own benefit, or that of our licensees.

### Other information

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#### Property, plant and equipment

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##### Leiden, the Netherlands (leased and owned)

Our corporate offices and research activities are located in a building of approximately 8,700 square meters (m<sup>2</sup>) in Leiden, the Netherlands. This building in Leiden includes 3,500 m<sup>2</sup> of laboratories, with BioSafety Level (BSL) 1, BSL 2 and BSL 3 labs. The remainder of the main building is divided into 2,800 m<sup>2</sup> of office space and 2,400 m<sup>2</sup> for storage,



## Information on the Company continued

technical areas, washrooms, waste destruction and sterilization. In addition, we lease 1,200 m<sup>2</sup> of office space adjacent to the corporate main building.

In 2008, the construction of the Valerio building, which was named after Crucell co-founder Dinko Valerio, was completed. The Valerio building is a GMP Process Technology Center of 5,400 m<sup>2</sup>. This new facility can be operated as a BSL 3 facility, in which two concurrent products can be produced at the BSL 2 and/or BSL 3 safety levels. The Valerio Building meets the highest environmental and safety standards recommended for the development activities to be conducted there. The facility has received approval from the Dutch government to produce material for use in humans.

### **Bern, Switzerland (owned)**

Crucell has two facilities located in the canton of Bern. These facilities are FDA/WHO/EMA approved and are the primary sites for the manufacturing of Inflexal V, Vivotif, MoRu-Viraten and Epaxal. The total floor space of is 45,000 m<sup>2</sup> for the combined facilities, 33,000 m<sup>2</sup> of which is manufacturing space. The facilities in Bern have the technology to manufacture both viral and bacterial vaccines using various manufacturing platforms within BSL 1 and BSL 2 environments. The Process Development group has a pilot plant of approximately 2,500 m<sup>2</sup>. This facility is GMP certified and allows for work to be carried out on BSL 2 products. The capabilities within this facility are cell banking, up and downstream manufacturing, formulation, filling and lyophilisation for bacterial vaccine production. This facility is currently being used for life cycle management activities and during 2009 was also used to conduct contract manufacturing activity for one of Crucell's partners.

### **Seoul, Korea (leased and owned)**

Our manufacturing facilities in Korea are KFDA/WHO approved and are used primarily for the production of Quinvaxem and Hepavax-Gene and for formulating and filling vials. The facilities include 3,200 m<sup>2</sup> of

production and development space, 1,300 m<sup>2</sup> of storage space and 1,800 m<sup>2</sup> of office space.

In October 2008, we announced that we will relocate the Korean production facility from Yongin City to the Incheon, Free Economic Zone. Construction activities at the new site started in December 2008 and are progressing well. First test runs are planned for the first half of 2010. The investments in the new facility are expected to total approximately € 50 million. The investment in the new production facility in 2009 amounted to € 33.6 million. The total floor space of the new facility is 19,000 m<sup>2</sup>.

### **Madrid, Spain (owned)**

Crucell has its main centre for filling and packaging operations in Madrid. Crucell's Spanish subsidiary is also responsible for distribution to the Spanish market. The facility is EMA approved and it has the capability to fill syringes on two filling lines, primarily used to fill Inflexal V and Epaxal. The total facility consists of 2,100 m<sup>2</sup> of manufacturing space, 1,000 m<sup>2</sup> of office/laboratory space and 2,600 m<sup>2</sup> of warehousing.

### **Stockholm Sweden (leased)**

In Sweden, our manufacturing facilities are EMA/WHO approved and are used for the production of Dukoral and the recombinant protein rCTB. The manufacturing capabilities consist of large scale cGMP manufacturing of bulk, comprising both bacterial and mammalian systems, formulation and filling, visual inspection and packaging in vials. The site has a total of 4,900 m<sup>2</sup> of GMP development and production space, 6,000 m<sup>2</sup> storage space and 2,700 m<sup>2</sup> of office space.

In August 2008, we announced the intention to move Dukoral and rCTB bulk production, formulation and fill/finish activities from Sweden to other sites within the Crucell organization. Following a detailed study to review the full scope of this move, it was decided to only move the formulation and filling activities to our Madrid site.

We also lease several offices at locations in the UK, Argentina, China, Italy, Spain and the US.

### Legal proceedings

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In the ordinary course of business, we have been and may become involved in disputes. Neither we, nor any of our subsidiaries, has been party to any legal or arbitration proceedings that may have, or have had during the 12 months preceding the date of this document, a significant effect on our results of operations or any of our subsidiaries nor, as far as we are aware, are any such legal proceedings pending or threatened, except for those disclosed in 'Intellectual Property – Patent Enforcement and Proceedings' in this section and those disclosed in section '5.19 Provisions, commitments and contingencies – legal proceedings' in the financial statements.

### Investments

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In 2009, € 51,035 was invested in property, plant and equipment compared to € 15,787 in 2008. The investments in 2009 mainly related to our new Korean production facility in the Incheon, Free Economic Zone.

In 2008, € 15,787 was invested in property, plant and equipment compared to € 27,156 in 2007. The investments in 2008 mainly related to our new Korean production facility in the Incheon, Free Economic Zone, investments in our facilities in Bern, Switzerland that will improve current production processes and allow in-house production of materials currently acquired from third parties and investments in our new filling line in Madrid, Spain.

### Raw materials

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We require a reliable supply of materials for the production of our products, including starting materials, like the serum-free medium in which we grow our PER.C6 cells, and antigens that are present in certain of our final products. Some of these materials are provided by a limited number of third party suppliers. Our ability to conduct research and to launch new products also depends on a steady supply of these raw materials. Any adverse changes to our existing supplier relationships will thus likely adversely affect our overall results. Prices for our raw materials are volatile and may change significantly over time. Some of our raw materials are purchased in foreign currencies and are subject to foreign currency exposures. We try to mitigate these exposures by entering in long term

purchasing arrangements and by hedging the foreign currency exposures on some of our purchases.

### Insurance

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We have in place general third party public and product liability insurance. Our policy has a limit of liability and has certain additional conditions to coverage and deductibles. We do not insure our phage antibody display library or PER.C6 master cell bank, though identical copies of the same cell bank are stored in multiple locations in Europe. We believe we carry adequate insurance relating to theft, fire and damage to the moveable assets within our facilities and other customary insurance coverage for most of our activities, including liability insurance coverage for the members of the Management Board, Management Committee and the Supervisory Board.

### Employees

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For a breakdown of the employees by function and geography reference is made to note 5.1 'Personnel expenses' in the financial statements.

### Dividends and dividend policy

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Crucell N.V. did not pay any dividends in 2009. We do not intend to pay dividends on our ordinary shares for the coming years, and thereafter only on the condition that our financial performance is adequate and it is in the shareholders' interest to pay dividends instead of investing the proceeds into the company. Any payment of future dividends and the amounts thereof will depend upon earnings, statutory and financial requirements and other factors deemed relevant by our Management Board, and will be subject to withholding tax in the Netherlands. In the event that we pay dividends in the future, holders of our American Depositary Shares (ADSs) will be entitled to receive payments in US dollars in respect of dividends on the underlying ordinary shares in accordance with a deposit agreement dated October 26, 2000 between The Bank of New York Mellon, as depository, and us.

# Risk factors

## Economic and industry-wide factors

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Various economic and industry-wide factors are relevant to the biotechnology industry. Biotechnology companies operate in a challenging market and are subject to high inherent business risk. A company's ability to bring novel products to the market is essential to long-term success. However, for a potential product the probability of reaching the market is low and the average development period can take up to ten years or more. Development costs for a single potential product are high and can range into the hundred of millions of Euro's. As a potential product moves through more advanced stages of R&D, the losses associated with failure will increase.

The biotechnology industry is subject to extensive government regulation, and companies must make significant expenditures to comply with these regulations. The business success of companies is dependent in a significant part on their ability to establish intellectual property rights, either internally or through licenses of third-party intellectual property rights, and protecting these intellectual property rights. For many biotechnology companies gathering the required capital in this market provides a challenge.

The biotechnology industry is internationally oriented and geographic boundaries have relatively limited impact on the development, distribution and marketing of products. This provides a world of opportunities, but also a world of competitors. Investing in biotechnology companies is about taking risks. Investors continue to be attracted by the high return possibilities. On a total market level the fundamentals of product development are sound and the prospects of the biotechnology industry are good.

## Our risk appetite

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The above circumstances are more or less equal to all biotechnology companies. What distinguishes Crucell are the choices that we make in transforming these risks into business opportunities. Crucell has an entrepreneurial spirit

and a 'can-do' mentality. We seek to maximize profits for stakeholders, but not at the cost of taking unwarranted risks. That is one of the main reasons why we think that risk management systems are crucial.

In 2006 we started to diversify our risks by acquiring several biotechnology companies. This transformed Crucell from a start-up company exclusively geared towards developing technologies into a fully integrated biotechnology company. This was the establishment of a Group that was able to generate cash to fund its research and development programs without the need to seek external financing as we are less dependent on capital markets.

Accelerated growth has been a theme for Crucell for several years and we have grown considerably over the years, but the Group considers the financial risks of expensive later phase development programs to be too high for a single company. We proactively seek partnerships with 'big pharma' companies and by sharing the risks and profits we believe that we can effectively reduce the jeopardy associated with failures. With the expertise of 'big pharma' companies in the areas of late stage clinical development, regulatory approval and large-scale production and the innovative power of Crucell, we expect these collaborations to be successful.

We consider the quality of our products to be essential. Supply interruptions, product recalls or inventory losses caused by unforeseen events such as manufacturing or distribution interruptions or regulatory actions, may have an adverse impact on our business as a whole. Therefore we have implemented a system of control measures to ensure the quality of our products, as failures in this area may have a wide pervasive impact on Crucell.

As the inherent business risks of the biotechnology industry are high, the Group seeks to mitigate financial risks where reasonably possible. Specifically, the Group has a conservative approach regarding its available cash. Our cash has been placed with solid financial institutions and has mainly short-term maturities. Consequently the Group accepts the marginal return on its cash resources. See note 3 'Financial

risk management' for more quantitative and qualitative disclosures of our financial risks

### **Our strategy, risk factors and risk management system**

It is our mission to protect human lives by bringing meaningful innovation to global health. Our strategy to develop products that address currently unmet medical needs, particularly in the field of infectious diseases. We develop, manufacture and market medical products combating a range of infectious diseases, focusing heavily—but not exclusively—on major health challenges in developing countries and emerging economies. The risk factors<sup>1</sup> identified below could prevent us from executing our strategy and reaching our objectives.

To safeguard the proper implementation and execution of our strategy we have an internal risk management and control system in place. Our Management Board is responsible for designing, implementing and operating the Company's internal risk management and control systems. The purpose of these systems is to manage in an effective and efficient manner the significant risks to which the Company is exposed. For a more detailed description please see 'Internal risk management and control system' in the Corporate Governance section of this Annual Report.

An integral part of our internal risk management process is the identification of risks that could prevent us from reaching our objectives. To identify these risks we performed a corporate risk assessment with the Disclosure Committee of the Company in 2009. The outcome has been discussed in the Audit Committee and was taken into account in the risk factors described below. We have classified these risk factors in accordance with the categories of objectives identified in the COSO model, an integrated internal control framework established by the Committee of Sponsoring Organizations of the Treadway Commission.

### **Strategic risks**

#### **Concentration of sales**

We are dependent on a limited number of products and customers for a majority of our revenues and expect this

dependence to continue in the foreseeable future. Our core product portfolio consists of eight vaccines, namely Quinvaxem, Hepavax-Gene, Epaxal Junior and MoRu-Viraten (paediatric vaccines), Inflflexal V (influenza vaccine), Dukoral, Epaxal and Vivotif (travel vaccines). The sales to our largest customers, which are in the paediatric vaccines area, represented a considerable part of our net product sales in 2009. In particular, we are highly dependent on sales of Quinvaxem and Inflflexal V. If these products were to become subject to any problem such as unexpected side effects, product liability litigation, loss of patent protection, supply interruptions, regulatory proceedings, publicity affecting doctor or patient confidence or pressure from competitive products, or if a new more effective treatment is introduced, we could experience a significant decrease in revenues and an adverse effect on our financial results. In particular, sales of Quinvaxem to our largest customer, UNICEF. Although UNICEF has renewed a long-term arrangement with us to purchase estimated quantities of Quinvaxem during the period 2010 through 2012, UNICEF is not obligated under that arrangement to purchase any minimum quantity of Quinvaxem from the Company. Sales of Quinvaxem to UNICEF are made pursuant to individual purchase orders. If UNICEF were to significantly decrease its purchases of Quinvaxem from us, this would result in a significant decrease in revenues and have an adverse effect on our financial results.

Additionally, our results may fluctuate as a result of seasonality in our business. In particular, the market for influenza vaccines is highly seasonal so a majority of our sales tends to occur in the second half of the year. Delays in production or distribution processes could result in a significant sales reduction.

#### **Strategic alliances**

If our current or prospective partners or licensees do not use our products or technologies, we may not be able to continue to realize revenues related to those partners or licensees. In particular, our current or prospective licensees or partners may use or develop alternative technologies or competing products, independently or in collaboration with others, including our competitors. If any of our licensees or partners becomes involved in a business combination or other major corporate transaction, this could cause a strategic shift in their business focus and lead them to discontinue the use of our products and technologies.

<sup>1</sup> The material risk factors listed below should be considered carefully. The risks we face are not limited to the risks listed here. Some risks are not yet known to us and some of the risks that we currently do not believe to be material to our operations could prove to be material at a later date. All of these risks can materially affect our business, financial condition and results of operations. Compliance and other risks are mainly addressing risks that apply to our Shareholders.

## Risk factors continued

Furthermore, we may have disagreements with our licensees over royalty payments owed to us and may have difficulty collecting these payments. Our existing license arrangements generally entitle us to receive royalty payments for any products developed using our technology. We depend on our licensees to inform us when they develop products using our technology. If our licensees fail to inform us of these developments, we may not otherwise learn of payments to which we are entitled. We may also incur significant expenses in collecting royalty payments, or in some instances, may not succeed in collecting these payments at all.

### Competition and pricing pressures

We face competition from other companies in the development, marketing and licensing of new technologies and products. We operate in competitive markets and compete with companies that have their own technologies, products or other forms of treatment for the diseases we target. Companies may develop proprietary positions in the areas of our core technologies or obtain regulatory approval for alternative technologies or commercial products earlier than we or our licensees do. Other companies, including our own licensees, may already have or may in the future develop products that are more effective or more effectively marketed and sold than those based on our technologies. We may not be able to compete effectively with these companies, and such competition could hamper our ability to bring products to market or to license and derive revenue from our technologies.

Our existing products may experience price pressure from competition with similar or other products on the market. Price pressure may further increase due to the introduction of new products, the expansion of production capacity, or decreases in demand. We cannot predict with accuracy the impact of such events on our revenues. Products that compete with Quinvaxem have already been introduced to the market and still others may yet be introduced increasing competition and price pressure on Quinvaxem.

Public markets for our products typically operate via a tender system. In a tender system, national governments or supranational organizations request proposals for the terms under which a vaccine manufacturer will provide a large quantity of one or more vaccines. The awarding of the contract is typically based on a number of factors, including price, supply reliability and product quality. Failure to win one of these public contracts may cause us to be ineligible to supply a national government or supranational organization for a period of time, resulting in a negative impact on our revenues.

### Operational risks

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#### Product development and clinical trials

All of our products and those of our licensees and partners may fail at any stage of development or even after market introduction due to factors beyond our control. Such failures could have a material adverse effect on our business and prospects.

Pre-clinical testing, clinical research and regulatory approval of a pharmaceutical or medical product is a very lengthy and costly process, and there is a significant risk of failure at each stage of the process should issues arise with respect to the efficacy or safety of a product. In particular, because pre-clinical and early clinical studies cannot ensure efficacy for humans, actual human studies are required for vaccine development. Such studies may, however, fail to prove the efficacy of the product candidates and are at constant risk of suspension for posing unreasonable health risks. There can be no assurance that any product candidate in our product pipeline will reach or successfully complete the clinical research phase of product development. Although a product that reaches a later stage of development offers a reasonably high probability of success relative to products in earlier stages, the chances of failure remain significant throughout the development process. We have had products fail at later stages of development in the past. Any or all of our current later-stage products could fail to be sufficiently safe or effective to be brought to market, or could otherwise fail to receive necessary regulatory approvals.

Even if the products currently in later-stage development are introduced to the market, there can be no assurance that demand for such products will develop or be sustained. If a market does develop, there can be no assurance that our existing facilities and resources will be sufficient to meet demand. Accordingly, there can be no assurance that we will realize any potential benefits that may be associated with our later-stage development product portfolio.

Our success depends on a sufficient pipeline of new products and technologies. We therefore commit substantial resources and efforts towards research and development. We have no assurance that these efforts will succeed. Failure to maintain a healthy flow of new products through our pipeline could result in higher costs without a proportional increase in revenues.

To continue to develop our core technologies and new products, we will need access to biological materials such as virus and tissue samples, which may be in limited supply. If we lose or do not obtain access to these biological materials, or if tighter restrictions are imposed on their use or on the information generated from their study, we could be restricted or prevented from conducting certain research and product development.

### **Interrupted product supply**

Supply interruptions, product recalls or inventory losses caused by unforeseen events such as manufacturing or distribution interruptions or regulatory actions, may reduce sales, delay the launch of new products and adversely affect our operating results and financial condition.

We require a reliable supply of materials for the production of our products, including starting materials, like the serum-free medium in which we grow our PER.C6 cells, and antigens that are present in certain of our final products. Some of these materials are provided by a limited number of third party suppliers. Our ability to conduct research and to launch new products also depends on a steady supply of these materials. Any adverse changes to our existing supplier relationships will thus likely adversely affect our overall results.

For Quinvaxem, four of the five antigen components are supplied to us by a third party. For Inflexal, we are fully dependent upon third party supply for the antigen. In the case of a flu pandemic, our suppliers may be forced to meet the requirements of certain governments, and therefore be unable to supply flu antigen to Crucell. For Epaxal, we

currently rely on a third party for the supply of one of the vaccine components.

Our products are manufactured and distributed using technically complex processes requiring specialized facilities, highly specific raw materials and other production constraints. The complexity of these processes as well as strict Group and government standards for the manufacture of our products may expose us to risks affecting our production process. Defects in the manufacturing process, including equipment malfunction, labor problems, regulatory action, power outages, natural disasters and environmental factors may all affect production output. The EU regulation (EC 1907/2006, REACH), requiring registration of all chemical materials by us and our suppliers, may cause supply interruptions of raw materials that may in turn cause production delays if we need to change our sources of certain raw materials. This regulation could further cause marketing delays as a result of complying with burdensome requirements to validate new suppliers. Our vaccine products in particular are subject to the risks of manufacturing problems and inventory loss because of the difficulties inherent in the manufacture of biological materials, whether in our own facilities or in the facilities of our suppliers. Vaccine components cannot be sterilized nor can preservatives be added to the manufactured vaccine. Contamination of our products could result in the loss of entire batches of finished vaccine, which could lead to lost sales, damage to customer relations, a significant outlay of time and money to investigate the cause of the contamination and possibly a costly product recall if contaminated vaccines have already been shipped to customers. A disruption in the supply of certain key products or our failure to accurately predict the demand for those products could have a material adverse effect on our results.

We generally rely on a separate facility for the manufacture of each of our products. The marketing and regulatory authorization of biological products, in particular vaccines, is strongly linked to the production facility and equipment that are used to manufacture those products. If an event occurs that interrupts production at one of our facilities we may have to transfer production to a new site, which would be costly and time consuming. Because of the short shelf life of biological products, our existing stocks of product may not be sufficient to supply our customers during such a transition period. For example, our manufacturing facility in Korea is our sole production source of the Quinvaxem vaccine. As such, we are vulnerable to any event that



## Risk factors continued

interrupts, reduces or slows production of Quinvaxem at that facility. We intend to relocate our Quinvaxem operations to another site in Korea and preparations for such a move are ongoing. The relocation of the Quinvaxem operations is a complex process, which includes the inherent risk of the new facility not coming online before the old one has shut down. We agreed on the time line and conditions of this relocation with parties involved, which should permit an efficient transition to the new production facility; however there can be no assurance that there will not be production delays as a result of the transition process.

### Regulatory approval

We may be unable to obtain regulatory approval to manufacture and market our new products or may have regulatory approval for the manufacture and marketing of our existing products revoked by regulatory bodies such as the US Food and Drug Administration (FDA), the European Medicines Agency (EMA), the European Commission or other non-governmental bodies such as the World Health Organization (WHO).

These various regulatory authorities have substantial discretion and may impose different conditions upon the marketing of a given product or may refuse to grant, or require additional data before granting, an approval to market a product even though the product may have already been approved by another regulatory authority. National and regional governments rely on the (pre)qualification and/or approval of biopharmaceutical products by evaluative bodies such as the WHO and, in some cases, simply elect not to purchase products which have not been granted (pre)qualification or approval.

Once a product is approved, its manufacture and marketing remains subject to regulatory requirements including industry code of conduct regulations. Changes in applicable regulations, breaches of regulatory requirements or the discovery of problems related to the marketing, manufacture, safety, quality, efficacy or stability of a product, as well as changes in the characteristics of a manufactured product stemming from alterations in its biological origins, could result in the imposition of fines or restrictions upon the

manufacture and sale of such product, including in the worst case scenario withdrawal of the product from the market altogether and/or the revocation of necessary regulatory approvals.

Regulators have granted certain of our products provisional or conditional marketing approval, requiring us to do follow-up studies to assess the safety and efficacy of the product in all or part of the target population. Poor results in any of these studies may give rise to the withdrawal of market authorization for some or all indications, in part or in all of the targeted population.

If regulatory authorities do not approve our new products or other products developed using our technologies, or if they subsequently revoke their approval, that may impact our revenues generated from the sale of products and/or the licensing of our technologies, which may in turn have a material adverse impact on our business, financial condition, results of operations and prospects.

### Intellectual property

Our efforts to protect our intellectual property rights or to defend ourselves against any claims of infringement of third party intellectual property may be costly and, if unsuccessful, we may be barred from using or licensing our technologies, and from developing and commercializing our new products.

Our commercial success depends in part on our ability to obtain and maintain adequate protection of our intellectual property rights, including patents, in our technologies and products in Europe, the US and elsewhere. Our patent-related activities do not afford complete protection to our intellectual property rights. Patents of technology-based enterprises like ours are subject to complex factual and legal issues that may give rise to uncertainty as to the validity, scope and priority of a particular patent. There can be no assurance that we will develop products that are patentable, that patents will be granted under pending or future applications or that patents granted to us or our collaborators will be of sufficient breadth to protect against competitors with similar technologies or products. A patent that is issued to us may be narrower

than our application or found to be invalid. Others may make attempts to copy, reverse engineer or design around aspects of our technology, or to obtain and use information that we regard as proprietary. In addition, our patent filings may be subject to challenges. Our inability to adequately protect our products and technologies in emerging economies, such as India and China, may give rise to competition in those countries from manufacturers operating in low-cost economies. Due to compulsory licensing regimes currently in place in many of these underdeveloped and developing jurisdictions, we may not be able to use our intellectual property rights to prevent the low-cost manufacture of competing products. Such competition may adversely affect our ability to maintain viable pricing levels and to sell products in those countries.

In addition, production of Quinvaxem requires a particular vaccine component that may become the subject of a patent dispute between either GSK and us or GSK and our supplier of that component. Although we believe that neither we nor our supplier would be held to have infringed or be infringing that patent, the outcome of legal disputes is invariably difficult to predict with accuracy, but in the event GSK were to prevail in infringement proceedings against us, this could materially adversely affect our business.

For a more detailed discussion of issues surrounding our patent enforcement and related proceedings, see 'Intellectual property – Patent enforcement and proceedings'.

We also endeavor to protect our proprietary technologies, processes, know-how and data by entering into confidentiality agreements with our employees, consultants, partners and certain contractors.

Our commercial success also depends on not infringing on the patents and other proprietary rights of third parties. As our activities in the biotechnology and biopharmaceutical markets expand and as more patents are issued in the field, the risk that our technologies and products may give rise to claims of alleged infringement increases. Licensing or other arrangements for addressing these infringements or violations may not be available, or may not be available on commercially acceptable terms if we or our licensees are unable to obtain licenses from third parties for the use of their intellectual property in the manufacture of our products, we or our licensees may be unable to develop or market those of our products which are based in part on the intellectual property of others.

### **Product liability exposure**

We may be exposed to product liability and other claims if third parties allege that our technologies or products have caused some harm.

If a third party sues us for an injury caused by our products or by products developed using our technologies, our liability could exceed our total assets. Because our vaccines that constitute our core products are administered to healthy individuals, any adverse health consequences associated with such administration may be more apparent and perceived as less tolerable than similar side effects associated with the treatment of disease.

Lawsuits against us arising out of clinical trials may increase as more and more licensees utilize our technologies, thereby reducing our control over the manner of their use. We maintain product liability insurance in respect of all of our marketed products. We may seek to obtain additional product liability insurance in the future, though such additional insurance may be prohibitively expensive, or may not cover all of our potential liabilities. If we are unable to obtain sufficient insurance coverage at an acceptable cost or if we are otherwise unable to protect ourselves against potential product liability claims, we and/or our licensees may be prevented or inhibited from commercializing new products.

Product liability cases, claims and even relatively minor potential health risks associated with our products may give rise to adverse regulatory action, and/or a negative market perception of us and our products, resulting in a material adverse effect on our business, financial condition, results of operations and prospects. Though we believe we have strong defenses in these and other cases, including patent infringement cases, the outcome of these matters could be negative and we could incur judgments or enter into settlements of claims that could have a material adverse effect on our results of operations.

### **Qualified personnel**

We may not be able to continue to recruit and retain highly qualified management, scientific, manufacturing, sales and marketing and finance personnel. Competition for qualified personnel could be intense and may limit our ability to attract and retain qualified personnel on acceptable terms and may therefore significantly increase our labor costs. The inability to attract and retain highly skilled personnel on acceptable terms could have a material adverse effect on our business, financial condition, results of operations and prospects.

## Risk factors continued

### Hazardous biological materials

Our manufacturing, research and development processes involve the controlled use of hazardous biological materials. Certain of our laboratory facilities are qualified up to Biosafety Level III (BSL-III), which allows us to work on-site with hazardous biological materials. Our operations may also produce hazardous biological waste. Given the inherently dangerous nature of certain biological materials we may work with in our BSL-III laboratory facilities, in spite of our best efforts we cannot eliminate the risk of accidental contamination or discharge or any injuries that result therefrom. Various laws and regulations govern the use, manufacture, storage, handling and disposal of these materials. We could be subject to civil damages and significant adverse publicity in the event of an improper or unauthorized release of, or exposure of individuals to, hazardous materials.

### Competition laws

We cannot be certain that our licensing or other agreements are not in breach of applicable competition laws and will not be rendered void by the relevant competition authorities. In the past, we have not notified the European Commission competition authorities of any of our licensing or other agreements or sought clearance from any other competition authority. We take the view that these agreements are unlikely to be found to infringe European Union or other applicable competition regulations. It is possible, however, that current or future licensing or other agreements of ours could be found to infringe applicable competition regulations. If so, among other things, we may be subject to fines and claims of damages and these agreements may be considered void and unenforceable. Under the European Union's 2004 Technology Transfer Block Exemption Regulation, we may be required to review and possibly amend existing license and technology transfer agreements in the future. For example, if certain market share thresholds will be or have been reached in the relevant markets by those third parties that use our technologies to produce their products, the Regulation may require us to revise our agreements with those parties to ensure the agreements are in compliance with applicable European competition law.

### Financial risks

#### Substantial use of capital

In the past, we have had to raise additional funds to acquire other companies and assets while continuing to research and develop our technologies and products. Although the Company generated positive cash flow in each of 2008 and 2009, we may have cash outflows and net operating losses in the future due to the occurrence of events that would consume our available capital resources. We may seek additional funding through public or private financing (including debt or equity financing), strategic alliances or other arrangements. We may not have access to additional financing and, if we do, it may not be on favorable terms. If we fail to raise sufficient funds, we may have to forego acquisitions, reduce our capital expenditures, scale back our product development, reduce our workforce and/or license products or technologies to others that we might otherwise commercialize ourselves.

#### Weakness in the global economy could negatively affect our business

The weakness of the global economy, which started in 2008 was a challenge for many companies worldwide. The ongoing financial crisis became prominent in September 2008 with the failure or near-failure of several United States and European based financial institutions and the resulting deterioration in financial and market conditions spread around the globe. The financial crisis has adversely affected businesses in many industries and geographical areas all over the world. The weakness of the global economy has not had a significant impact on our liquidity or on our ability to derive revenues from our operations. However, our liquidity may be affected by changes in global financial markets and global economic conditions.

Financial distress and bankruptcies experienced by our customers and suppliers resulting from the global economic slowdown could impair their ability to purchase our products, pay for products previously purchased or meet their obligations to us under supply agreements, as the case may be. This could lead to a material adverse effect on our revenues.

We do not know how long the current financial crisis will continue nor how severe it will ultimately be. In the long run, we may be affected if governmental agencies or supranational organizations decide to realign priorities and allocate fewer funds to public health initiatives. The financial crisis has had a negative effect on travel patterns, which is the key driver of sales of our travel vaccines. If that effect persists or worsens, it could have a material adverse effect on an important source of our revenues.

### **Foreign currency risk**

The majority of our total revenues in 2009 were in currencies other than our functional currency, the Euro. Currency fluctuations may cause significant economic foreign currency exposure and transactional foreign currency exposure. Fluctuations in the currencies in which we do business relative to the Euro have affected our results in the past and, given the current economic climate and the substantial fluctuations in interest rates and currency exchange rates, may do so again in the future. Notwithstanding our efforts to foresee and mitigate the effects of changes in fiscal circumstances, we cannot predict with certainty changes in currency and interest rates, inflation or other factors affecting our business. Because of the variability of currency exposures and the potential volatility of currency exchange rates, we may suffer significant foreign currency losses in the future, particularly if the Euro strengthens relative to currencies in which a significant number of our operations are conducted. We engage on a limited basis in derivative transactions to hedge our foreign currency exposure. See section 3.2 'Foreign currency risk' in the financial statements for further details on our foreign currency risk.

### **Taxation**

We are subject to the tax laws of the countries in which we operate as well as to European tax law. We may incur additional tax charges, including penalties, resulting from changes in tax laws or the interpretation of tax laws or from failure to comply with obligations required by relevant tax authorities. Disputes with tax authorities may arise with regard to the interpretation and application of tax laws. If any of these risks materializes, leading to tax costs associated with particular transactions being greater than anticipated, it could affect the profitability of our business as a whole. See note 5.4 'Income tax' in the financial statements for further details on our taxation.

## **Compliance and other risks**

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### **Ethical, legal and social issues related to the use of genetic technology**

The use of genetic technology and materials derived from human fetal tissue, such as our PER.C6 technology, may raise ethical, legal and/or social issues that could hinder regulatory approval, patentability or market acceptance of our technologies and the products developed using them. If these risks materialize they could have adverse consequences for our business since they could reduce or eliminate altogether potential markets for our own or our licensees' products.

### **Protective measures included in articles of association**

Protective measures included in our articles of association, in accordance with Dutch law, may prevent corporate action and/or shareholder transactions that might be in the best interests of our Company or the shareholders. Among other things, our articles of association provide that our Supervisory Board may make binding nominations for the election of its members. Only a shareholders' resolution approved by an absolute majority of the votes cast, representing more than one-third of our total outstanding shares, can override those nominations. Furthermore, under Dutch law, we may issue preference shares to a foundation, Stichting Preferente Aandelen Crucell, or the Preferred Foundation, giving it preferred dividend rights, which may dilute the voting rights held by the holders of other classes of shares. The Preferred Foundation has an option to acquire a number of preference shares equal to the number of our total outstanding shares. The chairman of our Supervisory Board, Jan Oosterveld, and four independent members comprise the board of the Preferred Foundation. These and other provisions in our articles of association may have the effect of delaying, deterring or preventing corporate action that might be in the best interest of the Company or our shareholders and/or preventing our shareholders from selling their ordinary shares or ADSs at a premium to the market price. See 'Other information' and 'Articles of Association and Share Capital' for additional information regarding the preference shares and our articles of association.

### **US and other non-Dutch holders of our ordinary shares may not be able to exercise pre-emption rights**

In the event of an increase in our share capital, holders of our ordinary shares are generally entitled to certain pre-emption rights unless these rights are excluded by a resolution of the General Meeting of Shareholders or a

## Risk factors continued

meeting of the Management Board if so delegated by the General Meeting of Shareholders. However, US holders of our ordinary shares may not be able to exercise pre-emption rights unless a registration statement under the Securities Act is declared effective with respect to the shares issuable upon exercise of such rights or an exemption from the registration requirements is available. No assurance can be given that any registration statement will be filed or, that if filed, it will be declared effective or that any exemption from registration would be available to enable the exercise of a US holder's pre-emption rights.

### **Shareholders may have difficulty protecting their interests as shareholders as we are a Dutch limited liability company**

Dutch law and our articles of association govern issues regarding the legal organization, internal constitution, corporate authority and liability of members of our Management Board and Supervisory Board. Most of our offices and assets are located outside the US. In addition, a majority of the members of our Supervisory Board, all of the members of our Management Board and management team are residents of, and most of their assets are located in, jurisdictions outside the US. As a result, it may be difficult to serve process on these persons within the US. It may also be difficult to enforce a US court judgment against them in a US court or in a Dutch court or to enforce a Dutch court's judgment against them in a US court. This can include actions under the US securities laws. In addition, it may be difficult to enforce, in original actions brought in courts in jurisdictions located outside the US, claims under US securities laws. For a more complete discussion of potential difficulties in protecting your rights, see 'Articles of Association and Share Capital – Enforcement of Civil Liabilities'.

### **Share price volatility**

Our ordinary shares and ADSs may have a highly volatile trading price. Shareholders may not be able to resell their ordinary shares or ADSs at or above the price they pay for them, the ADSs may vary in value and our share price may render us vulnerable to a takeover bid. The trading prices of ordinary shares of biotechnology companies in general have experienced significant volatility in the past and are likely to continue to be volatile. In addition, any negative change in the public's perception of the prospects of biotechnology companies could depress our ordinary share or ADS price regardless of our results of operations. Other broad market and industry factors, such as discussions on business combinations and a weak global economy may affect the trading price of our ordinary shares and ADSs, regardless of our performance.

# Operating and financial review and prospects

The following discussions should be read in conjunction with our financial statements and the notes thereto included elsewhere in this Annual Report. We refer to 'Forward-looking statements' as well as to 'Risk factors' for certain factors that may affect our operating results. Unless otherwise mentioned all amounts in this section are in thousands of Euro, except share and option data.

## General

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We are a fully integrated biopharmaceutical company, focused on developing, producing and marketing vaccines and antibodies against infectious diseases for private and public markets worldwide. We have a portfolio of well-known vaccines and a pipeline of potential new vaccines and antibodies. We combine proprietary technologies to discover, develop and produce a variety of vaccines and antibodies to combat infectious diseases.

## Summary of the full year financial results

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Total revenues and other operating income for the year ended December 31, 2009 were € 358,002, which represented a 26.4% increase over the € 283,309 in revenues and other operating income reported in 2008. The increase was mainly attributable to increased sales of paediatric vaccines and respiratory vaccines.

Total operating expenses amounted to € 124,377 (2008: € 130,119). R&D expenses of € 70,176 (2008: € 70,229) reflected our continued focus on lifecycle management of existing products and bringing our pipeline products to market.

We achieved profitability for the full year 2009, reporting a net profit of € 23,938, compared to a net profit of € 14,250 in 2008. This amounted to € 0.34 net profit per share in 2009, compared to a net profit per share of € 0.22 in 2008.

Cash and cash equivalents at December 31, 2009 amounted to € 327,837 (2008: € 170,969).

Our operating cash flow was € 76,866 positive in 2009, compared to a negative operating cash flow of € 254 in 2008. The increase was mainly due to the premium of € 68,455 allocated to the development programs as part of the strategic collaboration with JNJ. In addition, profit before tax increased by € 32,118. The increase was partly offset by an increase in working capital in an amount of € 27,749.

## Strategic collaboration with affiliates of Johnson & Johnson (JNJ)

The most important event of the year was the strategic agreement with affiliates of JNJ that we signed on September 28, 2009. Pursuant to the equity purchase agreement the Company issued 14,626,984 shares to JHC Nederland B.V., an affiliate of JNJ, at a price of € 20.63, totaling an amount of € 301,755. The number of shares issued represents 18% of the outstanding share capital of the Company after issuance.

Under IFRS the fair value of the equity investment corresponds with a total value of € 233,300. The fair value per share was equal to the price of a NYSE Euronext listed share of the Company at the date of issuance. Costs directly attributable to the issuance of shares amount to € 1,241 and are deducted from share premium, a component of equity. The premium over the fair value of € 68,455 has been allocated to the development programs that are part of the strategic collaboration with JNJ affiliates, and is presented as deferred income in the statement of financial position. This deferred income is recognized ratably over the period that the Group has continuing performance obligations during the development programs.



# Operating and financial review and prospects continued

## Segments

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We operate in one reportable segment, which comprises the development, production and marketing of products that combat infectious diseases. The Management Board is identified as the 'chief operating decision maker'. The Management Board reviews the consolidated operating results regularly to make decisions about resources and to assess overall performance.

## Retrospective application of newly adopted accounting policies

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As of January 1, 2009, we changed our accounting policy of recognizing actuarial gains and losses for our defined benefit pensions plans. The new policy requires that all actuarial gains and losses are recognized in other comprehensive income in the period in which they occur. Prior to this change all actuarial gains and losses arising from experience-based adjustments and changes in actuarial assumptions were accounted for in line with the 'corridor' method, which allowed deferral of these results. The new policy provides more relevant and timely information, because it requires an employer to recognize all transactions and events of a defined benefit postretirement plan in comprehensive income in the period in which they occur. The Group believes that this view is confirmed by recent developments in the International Accounting Standards Board (IASB) and current accounting regulations as issued by the Financial Accounting Standards Board (FASB), which propose to eliminate the smoothing and deferral mechanism of the "corridor" method.

In addition, the amount recognized in the statement of financial position can be reconciled more easily to the funded status of the defined benefit pension funds. For Cruell the only remaining difference between the funded status and the amount in the statement of financial position is the limitation on the defined benefit assets recognized due to the 'asset ceiling'.

The Group adjusted comparative amounts disclosed for each prior period presented as if the new accounting policy had always been applied. See note 1.5.1 'New adopted accounting policies in the financial year 2009' in the financial statements for further details on the change in accounting policy.

## Result of operations

### Revenues

The table below shows our revenues for each of the years in the three-year period ended December 31, 2009 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2009	2008	2007	09 vs. 08	08 vs. 07
Product sales	<b>304,439</b>	226,055	177,569	34.7	27.3
License revenues	<b>23,049</b>	30,202	12,211	(23.7)	147.3
Service fees	<b>10,675</b>	10,900	14,006	(2.1)	(22.2)
<b>Total revenues</b>	<b>338,163</b>	<b>267,157</b>	<b>203,786</b>	<b>26.6</b>	<b>31.1</b>

In 2009, total revenues increased by € 71,006 or 26.6% from € 267,157 in 2008 to € 338,163 in 2009. The increase is attributable to an increase in product sales of € 78,384 or 34.7%. The increase is partly offset by a decrease in license revenues of € 7,153 or 23.7% and revenue from service fees of € 225 or 2.1%.

In 2008, total revenues increased by € 63,371 or 31.1% from € 203,786 in 2007 to € 267,157 in 2008. The increase is attributable to an increase in product sales of € 48,486 or 27.3% and license revenues of € 17,991 or 147.3%. The increase was partly offset by a decrease in revenue from service fees of € 3,106 or 22.2%.

Export product sales constitute the majority of our total product sales. In 2009, domestic product sales amount to € 3,553 or 1.2% (2008: € 3,743 or 1.7% and 2007: € 717 or 0.4%). Almost all of our license revenues and service fees are billed to foreign parties.

Reference is made to note 4.4 'Geographical segments' in the financial statements for the breakdown of our revenues by geographic area.

### Product sales

Our product sales by type of product in 2009, 2008 and 2007, as well as the percentage change between the periods, are shown below:

In thousands of Euro

	Year ended December 31,			% Change	
	2009	2008	2007	09 vs. 08	08 vs. 07
Paediatric vaccines	<b>180,389</b>	111,039	77,371	62.5	43.5
Respiratory vaccines	<b>38,070</b>	32,474	33,188	17.2	(2.2)
Travel and endemic vaccines	<b>53,078</b>	55,572	47,282	(4.5)	17.5
Other products	<b>32,902</b>	26,970	19,728	22.0	36.7
<b>Total product sales</b>	<b>304,439</b>	<b>226,055</b>	<b>177,569</b>	<b>34.7</b>	<b>27.3</b>

#### 2009 compared to 2008

In 2009, product sales grew by € 78,384 or 34.7%. The increase was primarily attributable to increased sales of paediatric vaccines of € 69,350 or 62.5%, respiratory vaccines of € 5,596 or 17.2% and other products of € 5,932 or 22.0%.

## Operating and financial review and prospects continued

- The increase in sales of paediatric vaccines was mainly attributable to Quinvaxem. In 2009 we were able to continue to build on the growth achieved in 2008. Sales of Quinvaxem were 21.3 million units in 2007, 39.6 million units in 2008, and 64.3 million units in 2009. In August 2009 we announced a long-term arrangement with UNICEF to supply up to \$ 300 million worth of Quinvaxem for the period beginning 2010 through 2012. This is in addition to the \$ 500 million received during the period 2007 through 2009.
- The increase in sales of respiratory vaccines was principally a result of a strong flu season in 2009. Heightened awareness of influenza caused by the global 'swine flu' pandemic triggered an increase in the numbers of flu vaccinations administered worldwide, including vaccinations for seasonal epidemics.
- The increase in the other product sales categories was partially offset by a decrease in travel and endemic vaccines of € 2,494 or 4.5%. The financial crisis has had a negative effect on travel patterns, which is the key driver of sales of our travel vaccines.
- 'Other products' include vaccines and proteins products that we distribute on behalf of third parties and sales of conjugate products to Wyeth. The increase in sales of other products was mainly a result of increased sales of conjugates to Wyeth and increased sales of Prolastin under our distribution agreement with Talecris.

Our core product portfolio consists of eight vaccines: Quinvaxem, Hepavax-Gene, Epaxal Junior and MoRu-Viraten (paediatric vaccines), Inflexal V (respiratory), Dukoral, Epaxal and Vivotif (travel and endemic vaccines). The aggregate revenues for our core product portfolio amounted to € 265,384 in 2009 (2008: € 191,631, 2007: € 151,791) and represented 87.2% (2008: 84.8%, 2007: 85.5%) of our total product sales.

In 2009, sales to our two largest customers, which are in the paediatric vaccines area, amounted to € 148,072 or 48.6% and € 21,013 or 6.9% of net product sales. In 2008, sales to these customers accounted for € 85,142 or 37.6% and € 18,390 or 8.1% of net product sales, respectively.

### *2008 compared to 2007*

In 2008, product sales grew by € 48,486 or 27.3% compared to 2007. The increase is primarily attributable to increased sales of paediatric vaccines of € 33,668 or 43.5%, travel and endemic vaccines of € 8,290 or 17.5% and other products of € 7,242 or 36.7%.

- Paediatric vaccines grew mainly due to increased Quinvaxem sales. In 2008, supranational organizations awarded us additional contracts for Quinvaxem and Hepavax Gene amounting to \$ 270 million for the period 2008-2009, in addition to the initially received award of \$ 230 million in December 2006.
- Travel and endemic vaccines showed considerable growth on an overall basis.
- The increase in other products by € 7,242 or 36.7% mainly relates to increased sales under our distribution agreement with Talecris as 2008 includes a whole year of sales under this agreement for the first time.

### **License revenues**

In 2009, license revenues decreased by € 7,153 or 23.7% to € 23,049, compared to 2008. License revenues include a milestone and partial amortization of the deferred income in connection with our strategic collaboration with JNJ and royalty payments received from Shanta, an Indian manufacturer of vaccines. The decrease compared to last year is mainly due to one-off milestone payments, in the amount of € 14.0 million from sanofi pasteur relating to our rabies development program in 2008.

In 2008, license revenues increased by € 17,991 or 147.3% to € 30,202 compared to 2007. This increase mainly results from milestone payments related to the rabies and influenza programs from sanofi pasteur and upfront fees received from Talecris for the exclusive production rights of two specific proteins.

### Service fees

In 2009, service fees amounted to € 10,675, a decrease of € 225 or 2.1% compared to 2008. Total revenue streams relating to service fees were relatively stable for the year. Service fees include revenues relating to various collaboration agreements of the Company. Typically we do not retain any residual interest on products developed under these agreements.

In 2008, service fees amount to € 10,900, a decrease of € 3,106 or 22.2 % compared to 2007. In 2008, service fees on the sanofi pasteur influenza project were less compared to 2007. Service fees include revenues relating to various collaboration agreements.

### Cost of sales

The following table shows our cost of sales for each of the years in the three-year period ended December 31, 2009 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2009	2008	2007	09 vs. 08	08 vs. 07
Cost of product sales	<b>185,599</b>	138,790	124,557	33.7	11.4
Cost of service fees and license fees	<b>9,014</b>	6,965	10,327	29.4	(32.6)
<b>Total cost of sales</b>	<b>194,613</b>	<b>145,755</b>	<b>134,884</b>	<b>33.5</b>	<b>8.1</b>

### Cost of product sales

Costs of product sales comprise direct labor, materials, and overhead costs incurred in performing work under various collaboration agreements directly related to product sales.

The cost of product sales increased in 2009 mainly due to an increase in product sales of 34.7%. The gross margin on product sales amounted to 39.0% in 2009 (2008: 38.6%). There were two distinct developments in the gross margin percentage. Positive gross margin effects were caused by larger scale production efficiencies and improved yields in the production process. These positive effects were almost fully offset by negative currency effects in 2009. The strengthening of the functional currencies in production countries increased our local cost-base (Korean Won and Swiss Franc).

The cost of product sales increased in 2008 mainly due to an increase in product sales of 27.3%. This increase was partly offset by the reduction in purchase price allocation charges in 2008. The 2008 cost of product sales includes additional expenses of € 3,473 (2007: € 10,191) relating to the purchase price allocations of the businesses acquired by the Group. The gross margin on product sales amounts to 38.6% (2007: 29.9%). The percentage increase in gross margin is mainly due to the strengthening of the US Dollar in the second half of 2008, product-mix changes, improvements in production performance and a reduction of the purchase price allocation charges in 2008.

### Cost of service fees and license fees

Cost of service fees comprises direct labor, materials and overhead costs related to work under various collaboration agreements. We do not retain the residual interest on products developed under the agreements and will normally not have ownership of intellectual property rights on these products. Service contracts include different types of contractual relationships; consequently margins may vary significantly from year to year.

In 2009, the cost of service fees increased by € 2,049 or 29.4 % compared to 2008. The increase was mainly caused by a limited number of contracts. The gross margin on service fees was 15.6% in 2009 compared to 36.1% in 2008. The reduction

## Operating and financial review and prospects continued

is mainly caused by lower margins on the above contracts. The margin can vary significantly as the service fees include a wide range of services with different risk profiles and corresponding rewards.

In 2008, the cost of service fees decreased by € 3,362 or 32.6 % compared to 2007. The decrease reflects the lower level of service fee revenues, which reduced our expenses. The gross margin on service fees was 36.1% in 2008 compared to 26.3% in 2007.

### Other operating income

The following table shows our other operating income for each of the years in the three-year period ended December 31, 2009 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2009	2008	2007	09 vs. 08	08 vs. 07
Government grants	<b>6,870</b>	5,380	7,086	27.7	(24.1)
Other income	<b>12,969</b>	10,772	2,244	20.4	380.0
<b>Total other operating income</b>	<b>19,839</b>	<b>16,152</b>	<b>9,330</b>	<b>22.8</b>	<b>73.1</b>

### Government grants

In 2009, revenue from government grants increased by € 1,490 or 27.7% compared to 2008. This was mainly due to additional funding from the NIH in relation to our influenza antibodies program, our program to develop a new adenovirus vector-based vaccine against HIV/AIDS, as well as our Ebola and Marburg development program.

In 2008, government grants decreased by € 1,706 or 24.1% compared to 2007. The grants decreased as several projects were completed in 2007. The most significant grants in 2008 were received from NIH and from SenterNovem, an agency of the Dutch Ministry of Economic Affairs, for numerous research projects.

### Other income

Other income mainly consists of the reimbursement of development costs and funding received from non-governmental agencies and/or our program partners. Other income also includes non-core business transactions such as the sale of property, plant and equipment and income generated from training courses. Other income increased by € 2,197 or 20.4% to € 12,969 in 2009 (2008: € 10,772) mainly due to increased funding received from sanofi pasteur in relation to our rabies program as well as increased funding from MVI/ PATH in relation to our malaria program.

In 2008, other income increased by € 8,528 or 380.0% mainly due to reimbursement of development costs on the rabies program, for which the partnership with sanofi pasteur started in 2008, and increased funding from non-governmental agencies in 2008.

## Other operating expenses

The following table shows our other operating expenses for each of the years in the three-year period ended December 31, 2009 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% -Change	
	2009	2008	2007	09 vs. 08	08 vs. 07
Research and development	<b>70,176</b>	70,229	63,995	(0.1)	9.7
Selling, general and administrative	<b>61,400</b>	64,778	63,566	(5.2)	1.9
(Reversal of) Impairment	<b>(7,199)</b>	(4,888)	171	47.3	(2,958.5)
<b>Total other operating expenses</b>	<b>124,377</b>	<b>130,119</b>	<b>127,732</b>	<b>(4.4)</b>	<b>1.9</b>

### Research and development expenses

Research and development expenses consist of personnel expenses, laboratory expenses, technology purchases, patent related fees, technology license fees, depreciation of property, plant and equipment and amortization of intangible assets related to research and development, and lease expenses for lab space and equipment lease. Research and development expenses also include fees we pay to third parties who conduct research on our behalf.

Research and development expenses remained stable on total level as the expenses decreased by € 53 or 0.1%.

- Innovation and discovery expenses decreased in an amount of € 1,228 or by 5.3%. The decrease is the result of a more selective focus on early-stage programs. The decrease was partially offset by increased in research expenditures for our flu-mAb program, which was accelerated following our collaboration with JNJ.
- Development expenses decreased by € 175 or 0.8%. The expenses remained stable on total level, but there was a shift in expenditures between programs. Rabies expenditures were lower due to reduced expenditure on clinical trials compared to 2008. Development expenditures on, among others, malaria and tuberculosis increased.
- The remaining costs in research and development expenses increased by € 1,350. These costs include among others quality control expenses, lifecycle maintenance and general research and development support.

Research and development expenses increased in 2008 by € 6,234 or 9.7% compared to 2007. This increase is mainly attributable to increased expenditures on the rabies program for which two Phase II clinical trials were performed.

Research and development expenses comprised 54.0% of total other operating expenses in 2008 (2007: 50.1%). We expect that research and development expenses will continue to be a significant portion of our overall expenses in the future.

### Selling, general and administrative expenses

Selling, general and administrative expenses consist of personnel expenses and other operating expenses in marketing & sales, finance, human resources, investor relations, legal and general management.

These expenses decreased in 2009 by € 3,378 or 5.2% to € 61,400 in 2009 compared to € 64,778 in 2008. This decrease was primarily due to lower selling expenses resulting from our Healthy Ambition program, which targeted among others sales and marketing efficiency gains.

These expenses increased in 2008 by € 1,212 or 1.9% to € 64,778 in 2008 compared to € 63,566 in 2007. This increase is primarily due to the overall growth of the Group as a whole. Specific items are the increased distribution and sales expenses as a result of increased revenues, annual salary increases and the recognition of specific provisions. The increase in selling, general and administrative programs is partly offset by cost reductions realized through our Healthy Ambition program.



# Operating and financial review and prospects continued

## Impairment

In the third quarter of 2009, the Group reversed an impairment of € 8,084 relating to two buildings in Bern, Switzerland. The buildings were impaired in the fourth quarter of 2006 as there was no direct use for them. The buildings are now being used as development production sites for Epaxal and our tuberculosis program. The buildings have been adapted to the specific needs of the development programs, which avoided major spending in the construction of new development facilities.

In 2009, there were several smaller impairments in Switzerland, Sweden, the Netherlands and Korea for individual items of property, plant and equipment totaling to an amount of € 885.

In the first quarter of 2008, we reversed € 5,219 of previously impaired property, plant and equipment. In 2008, we entered into an exclusive agreement with Wyeth Pharmaceuticals in which we developed and manufactured certain components of a vaccine for use by Wyeth in clinical studies. The contract manufacturing takes place in one of the two buildings that were originally impaired in 2006. We reassessed the recoverable amount of the asset and as the outcome exceeded the carrying value of nil, we partially reversed the previously recognized impairment loss on this building.

In the fourth quarter of 2008, we recognized an impairment charge of € 331 for the animal housing facility in Bern, Switzerland that was not in use anymore. As there was no alternative use for this building for any of the Group's other activities and the building cannot be sold directly to other parties as it is on our campus, the Group impaired the carrying value to zero.

## Operating profit/ (loss)

The following table shows our operating profit/ (loss), for each of the years in the three-year period ended December 31, 2009 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2009	2008	2007	09 vs. 08	08 vs. 07
<b>Operating profit / (loss)</b>	<b>39,012</b>	<b>7,435</b>	<b>(49,500)</b>	<b>424.7</b>	<b>(115.0)</b>

The movements in operating profit/ (loss) are explained by the operating results discussed above.

### Financial income and expense, net

The following table shows our financial income and expenses, net, for each of the years in the three-year period ended December 31, 2009 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2009	2008	2007	09 vs. 08	08 vs. 07
Financial income and expenses	<b>(3,193)</b>	(2,662)	1,378	(19.9)	(293.2)
Results investments non-consolidated Companies	<b>2,147</b>	(128)	(996)	1,777.3	87.1
Gain on disposal of non-consolidated Companies	—	1,570	2,186	(100.0)	(28.2)
Disposal of subsidiaries	—	(367)	—	—	—
<b>Total financial income and expenses</b>	<b>(1,046)</b>	<b>(1,587)</b>	<b>2,568</b>	<b>34.1</b>	<b>(161.8)</b>

### Financial income and expenses

Financial income and expenses mainly consist of interest income and expenses, foreign exchange losses and other financial expenses.

In 2009, the negative result in net financial income and expenses totaled € 3,193 in 2009 (2008: € 2,662), consisting of interest income of € 2,429, net foreign exchange losses of € 2,324, interest expenses of € 2,949 and other financial expenses of € 349.

The net financial expenses increased in 2009 by € 531 or 19.9 % compared to 2008. The increase in financial expenses was primarily attributable to reduced interest income in an amount of € 2,592 caused by lower interest rates in 2009.

The increase was partly offset by reduced foreign exchange losses of € 1,602 as the Group adopted a more proactive approach on hedging foreign currency transaction exposures. (See note 3.2 'Foreign currency risk' in the financial statements for more details on foreign currency risk management including the use of hedging instruments by the Group); and reduced other financial expenses of € 689 as a result of our decision not to factor trade receivables in 2009.

In 2008, the negative result on net financial income and expenses totaled € 2,662 and consists of interest income of € 5,021, foreign exchange losses of € 3,926, interest expenses of € 2,719 and other financial expenses of € 1,038.

The net financial income and expenses decreased by € 4,040 or 293.2 % compared to 2007. The decrease is primarily attributable to:

- Foreign exchange losses of € 3,926. These losses mainly resulted from a weaker Euro in conjunction with Euro receivables in Switzerland, as the Swiss Franc is the functional currency of our Swiss subsidiary. In addition, foreign exchange losses were realized on Euro liabilities and losses on US Dollar transactions in Korea;
- Reduction of interest income by € 690, mainly caused by a lower average cash balance in 2008 compared to 2007;
- Increased interest expenses of € 438 as a result of increased finance leases and short-term financial liabilities; and
- Increase other financial expenses of € 292 primarily due to factoring arrangements engaged in during 2008.

### Results investments non-consolidated companies

At December 31, 2009, we had one associate, ADImmune Corp and one joint venture partner, Percivia. The results of investments in non-consolidated companies are accounted for under the equity method and amounted to a total gain in 2009 of € 2,147 (2008: loss of € 128). The increase of € 2,275 compared to 2008 year is mainly due to the positive results of ADImmune Ltd. in 2009.

## Operating and financial review and prospects continued

In July 2008, we sold our investment in Kenta Biotech AG. The results of investments in non-consolidated companies include the results of Kenta Biotech AG up to the moment of the sale. In 2008, the results of investments in non-consolidated companies amount to a total loss of € 128 (2007: € 996). The decrease of € 868 or 87.1% compared to 2007 year is mainly due to the reduced losses on Kenta Biotech AG.

### Results on disposal non-consolidated companies

No non-consolidated companies were sold in 2009.

On July 3, 2008 the Group sold all of the 2,625,000 shares it owned in Kenta Biotech AG to Ingro Finanz AG. Prior to this sale, our ownership interest had already been diluted from 37% in 2006 to 22% by the end of 2007. We realized an accounting gain in 2008 of € 1,570 on the sale.

### Disposal of subsidiaries

No subsidiaries were sold in 2009.

In November 2008, we sold our fully-owned subsidiary Etna Biotech Srl to Zydus Cadila. The sale resulted in net proceeds of € 182 and an accounting loss on disposal of € 367.

### Income tax

The table shows our income tax for each of the years in the three-year period ended December 31, 2009 and the percentage change between these periods.

In thousands of Euro

	Year ended December 31,			% Change	
	2009	2008	2007	09 vs. 08	08 vs. 07
<b>Income tax</b>	<b>(14,028)</b>	<b>8,402</b>	<b>2,598</b>	<b>(267.0)</b>	<b>223.4</b>

### 2009

In 2009, the tax charge amounted to € 14,028 compared to a tax income of € 8,402 in 2008. The increase of the tax charge in an amount of € 22,430 was mainly caused by:

- increased profitability of our subsidiaries in Switzerland and Korea in 2009;
- recognition of carry forward losses by our Swiss subsidiary in 2008 that were previously unrecognized; and
- a reduction of the expected tax realization rate on our deferred tax liabilities in Korea in 2008.

The Group had an effective tax rate of 36.9% in 2009. Our effective tax rate was impacted by numerous items. The effective tax reconciliation starts with our IFRS profit/ (loss) per subsidiary multiplied by the domestic rate of tax in the country in which our subsidiaries are domiciled. Based on this calculation the 2009 tax charge would have been € 2,764. The difference between the actual tax charge of € 14,028 and the calculated tax charge of € 2,764 is mainly explained by the following transactions:

- In the Netherlands, under IFRS, we realized losses in the amount of € 44,368 (excluding dividends from subsidiaries). No deferred tax assets were recognized for these losses and on other temporary differences between valuation for tax purposes and IFRS purposes. Not recognizing deferred tax assets in the Netherlands had a negative impact on taxation of € 9,719.
- Non-deductible stock-option expenses are recognized in the Netherlands in a net amount of € 1,837 in 2009 (2008: € 1,251).

See note 1.4 'Use of estimates and judgments' in the financial statements section for a description of estimates and management judgments in determining the tax position and note '5.4 Income tax' in the financial statements for a numerical reconciliation of our effective tax rates.

### 2008

In 2008, our total profit under IFRS of € 5,848 had a negative correlation with our total taxes based on domestic rates of € 820. This negative correlation was mainly caused by a loss under IFRS in our Dutch operation at a tax rate of 25.5% and a profit of our Korean subsidiary at a lower average tax rate of 21.0%.

In addition, the following transactions significantly affected our effective tax rate reconciliation:

- In the Netherlands, under IFRS, we generated loss in an amount of € 29,710 (excluding dividends from subsidiaries). No deferred tax assets were recognized for these losses and on other temporary differences between valuation for tax purposes and IFRS purposes. Not recognizing deferred tax assets in the Netherlands had a negative impact on taxation of € 6,103;
- We reassessed the valuation of our carry forward losses and recognized previously unrecognized carry forward losses in our subsidiary Berna Biotech AG, which resulted in a taxation gain of € 8,585;
- As of the year 2012, we will benefit from a tax holiday to our investment in the Incheon, Free Economic Zone, Korea, which will significantly reduce the effective Korean income tax rate for a period of 5 years. The reduced expected realization rate for our deferred tax liabilities in Korea resulted in a taxation gain of € 3,384;
- In 2008, we benefited in Korea from a research and development tax credit for an amount of € 2,916; and
- Non-deductible stock-option expenses are recognized in the Netherlands in a net amount of € 1,251 in 2008.

### Liquidity

We have a strong cash position, which we believe makes it possible to continue financing important development programs. Our cash and cash equivalents amounted to € 327,837 and € 170,969 as of December 31, 2009 and 2008, respectively. We believe that our liquidity is sufficient for our present requirements.

On September 28, 2009 we entered into a strategic agreement with JNJ that resulted in net proceeds of € 301,755 in return for 18.0% of the Company's outstanding ordinary shares (after issuance) and the strategic collaboration on several development programs. An amount of € 100,000 was invested in short term deposits with maturities over 3 months. These deposits are classified as current financial assets instead of cash.

### Day sales outstanding

The day sales outstanding (DSO) calculated on the basis of year-end accounts receivable and full year product sales indicated that the average DSO increased from 64 days as at December 31, 2008 to 93 days as at December 31, 2009. We note that there have been no material changes to our payment terms or to our payment collection processes. The increase was mainly due to the absence of factoring arrangements in 2009. Following the collaboration with JNJ our cash position improved significantly. Given these circumstances we made the choice not to enter in relatively expensive non-recourse factoring arrangements. In 2008, we entered into factoring arrangements in an amount of € 25,993, as discussed below. Without these factoring arrangements the DSO would have been 105 as at December 31, 2008.

## Operating and financial review and prospects continued

In 2008, the calculated average DSO decreased from 96 days as at December 31, 2007 to 64 days as at December 31, 2008. The decrease was mainly due to an increase in derecognition of accounts receivable related to factoring arrangements:

- In 2008, we entered into factoring arrangements relating to certain Italian customers that allowed derecognition of accounts receivable in an amount of EUR 11,107. This factoring arrangement resulted in a decrease of 18 days in the calculation of the DSO. In 2007, we also entered into factoring arrangements with respect to Italian customers for an amount of EUR 5,653. However, these 2007 factoring arrangements did not lead to derecognition as we assessed that not all risks and rewards were transferred. The 2007 cash receipts were accounted for as short term financial liabilities.
- Prior to the end of 2007 and 2008, we entered into factoring arrangements with a third party to sell a portion of our receivables from December's product sales to a supranational organization. Consequently accounts receivables outstanding from this customer were relatively low as at the end of the years 2007 and 2008. The increase in revenues in 2008 compared to 2007 attributable to sales to this supranational organization did not lead to a significant increase of trade accounts receivable outstanding as at year-end, but did cause the average DSO to decrease by 19 days.

### Cash flows

The following table shows our statement of cash flow for each of the years in the three-year period ended December 31, 2009 and the percentage change between these periods.

In thousands of Euro

	2009	2008	2007	09 vs. 08	08 vs. 07
Profit/ (loss) of the period	<b>23,938</b>	14,250	(44,334)	68.0	132.1
Adjustments for non-cash items	<b>33,121</b>	19,137	46,017	73.1	(58.4)
Changes in net working capital	<b>(27,749)</b>	(29,814)	25,170	6.9	(218.5)
Receipt from (payments of) deferred income and provisions	<b>54,167</b>	(567)	(962)	9,653.3	41.1
Interest and taxes paid	<b>(6,611)</b>	(3,260)	(3,697)	102.8	11.8
<b>Net cash flows from/ (used in) operating activities</b>	<b>76,866</b>	<b>(254)</b>	<b>22,194</b>	<b>&gt;9,999</b>	<b>(101.1)</b>
<b>Net cash flows from/ (used in) investing activities</b>	<b>(154,387)</b>	<b>(8,907)</b>	<b>(24,241)</b>	<b>(1,633.3)</b>	<b>63.3</b>
<b>Net cash flows from financing activities</b>	<b>231,512</b>	<b>16,626</b>	<b>11,244</b>	<b>1,292.5</b>	<b>47.9</b>
Total cash flow	<b>153,991</b>	7,465	9,197	1,962.8	(18.8)
Effect of exchange rates on cash and cash equivalents	<b>2,877</b>	256	(3,786)	1,023.8	106.8
<b>Net increase/ (decrease) in cash and cash equivalents</b>	<b>156,868</b>	<b>7,721</b>	<b>5,411</b>	<b>1,931.7</b>	<b>42.7</b>
Cash and cash equivalents at beginning of period	<b>170,969</b>	163,248	157,837	4.7	3.4
Cash and cash equivalents at end of period	<b>327,837</b>	170,969	163,248	91.8	4.7

### Net cash flows from/ (used in) operating activities

#### 2009

In 2009, our operating cash flow was € 76,866 positive, compared to a negative operating cash flow of € 254 in 2008. This positive cash flow resulted from numerous cash flows. In 2009, the most significant cash flows from operating activities resulted from:

- the premium in an amount of € 68,455 over the fair value of the shares on the 18% equity investment by JNJ allocated to the development programs. The non-current amount of € 51,341 is included in the 'Receipt (payments) deferred income and provisions' and the current amount of € 17,114 is included in the 'Changes in net working capital';
- the Group's profit before tax increased by € 32,118 compared to 2008; and
- cash flows related to inventories were € 15,646 lower compared to 2008.

The increase was partly offset by increased trade accounts receivable. Cash flows related to trade accounts receivable were € 42,021 higher in 2009 compared to 2008. In 2009, we did not enter into factoring arrangements, whereas in 2008 we signed factoring arrangements with a value of € 25,993. Furthermore, product sales increased by 19% during the fourth quarter of 2009 compared to the same quarter prior year, which also caused the accounts receivable to increase.

## **2008**

In 2008, our net cash flow from operating activities decreased by € 22,448 or 101.1% compared to 2007. The decrease resulted from an increase of our working capital by € 54,589 and a reduction in the adjustments for non-cash items by € 26,880. The decrease is partly offset by € 58,584 due to improved results in 2008 compared to 2007.

In 2008, the decrease in changes in the net-working capital compared to 2007 amounted to € 54,589. The year 2008 had relatively stable cash flows on the monetary working capital items compared to positive cash flows in 2007. The decrease in 2008 compared to 2007 mainly resulted from inventories for € 30,993 due to build-up of Quinvaxem inventory for 2009 sales, and other current liabilities for € 22,327.

In 2008, adjustments for non-cash items were reduced by € 26,880. This reduction was mainly caused by:

- One-off cash receipts in 2007 in the amount of € 11,500 in 2007 relating to the non-current deferred revenue on the ADImmune technology license and the rabies program;
- Non-cash revenues realized in 2008 for an amount of € 4,728 that related to the above transactions; and
- Partial reversal of the impairment loss on one of our buildings in Switzerland in 2008 for an amount of € 5,219 as we now perform contract manufacturing at this location.

## **Net cash flows from/ (used in) investing activities**

### **2009**

Our cash flow used in investing activities amounted to € 154,387 in 2009, compared to € 8,907 in 2008.

In 2009, the most significant cash flows used in investing activities resulted from:

- an amount of € 100,000 was invested in deposits with a maturity over 3 months.
- investments made in property, plant and equipment for an amount of € 51,035. These investments mainly related to our new Korean production facility and investments in our facilities in Bern, Switzerland that will improve current production processes and allow in-house production of materials currently sourced from third parties.
- investments made in intangible assets in an amount of € 5,925.

In 2009, the most significant cash flows from investing activities were from interest received on cash and cash equivalents and other financial assets of € 2,254 in 2009 (2008: € 4,395).



# Operating and financial review and prospects continued

## 2008

Our cash flow used in investing activities amounted to € 8,907 in 2008, compared to € 24,241 in 2007.

In 2008, the most significant cash flows used in investing activities resulted from:

- investments made in property, plant and equipment for an amount of € 15,787. These investments mainly related to our new Korean production facility, investments in our facilities in Bern, Switzerland that will improve current production processes and allow in-house production of materials currently acquired from third parties, as well as investments in our new filling line in Madrid, Spain.

In 2008, the most significant cash flows from investing activities were from the following transactions:

- Interest received of € 4,395 in 2008 (2007: € 5,274);
- The sale of all shares owned by the Group in Kenta Biotech AG for € 1,570 to Ingro Finanz AG; and
- Restricted deposits that were transferred to cash and cash equivalents for € 1,500.

## Net cash flows from/ (used in) financing activities

### 2009

In 2009, the total cash flow from financing activities amounted to € 231,512 in 2009, compared to € 16,626 in 2008.

In 2009, the most significant cash flows from financing activities resulted from:

- the issuance of 14,626,984 shares to JHC Nederland B.V. an affiliate of JNJ, at a price of € 20.63 totaling an amount of € 301,755. For accounting purposes the Group determined the fair value of the shares to be € 233,300. Net proceeds, after deducting directly attributable transaction costs, amounted to 232,059 (gross: € 233,300);
- cash proceeds resulting from share based payment transactions, mainly the exercise of options by employees, amounted to € 9,206 in 2009;
- an amount of € 2,884 was drawn under a KRW denominated mortgage loan facility by the Group's Korean subsidiary in connection with the new production facility.

The increase in the cash flows from financing activities was partly offset by the following cash flows used in financing activities:

- Redemption of an unsecured Euro-denominated loan by Berna Biotech Corp. in Korea for € 2,909;
- A partial redemption of a KRW denominated flexible loan, also in Korea, for € 6,757; and
- Repayment of finance lease liabilities in the aggregate amount of € 2,984.

### 2008

In 2008, the total cash flow from financing activities amounted to € 16,626 in 2008, compared to € 11,244 in 2007.

In 2008, the most significant cash flows from financing activities resulted from:

- Additional short-term financing facilities in Korea for an amount of € 22,222; and
- Finance leases with proceeds of € 12,368 relating to our GMP-facility in Leiden, the Netherlands and our Spanish filling-line.

The most significant cash flows used in financing activities mainly related to:

- Redemption of a Korean Won-denominated privately placed bond in Korea for € 11,869 and a partial redemption of a short-term Euro loan also in Korea for € 1,455;
- Settlement of financial liabilities relating to factored Italian trade accounts receivable by € 5,653 for which the Group did not substantially transfer all the risks and rewards in 2007; and
- Repayment of finance lease liabilities for an amount of € 1,922.

### Critical accounting policies and estimates

The methods, estimates and judgments we use in applying our most critical accounting policies have a significant impact on the results we report in our financial statements. Please see note 1.4 'Use of estimates and judgments' in the financial statements for further details on our most critical policies and the methods, estimates and judgments used.

In addition to the critical accounting policies and estimates, the Group chooses to disclose the impact of discounts, rebates and returns.

### Discounts, rebates and returns

At the time sales revenue is recognized, we also record estimates for revenue deductions, including discounts, rebates and product returns. We report net sales after deducting all sales deductions from gross sales revenue. The following table identifies the items that reduced our gross product revenue as at the end of the periods ended December 31, 2009, 2008 and 2007.

In thousands of Euro

	2009	2008	2007
Product sales, gross	<b>305,758</b>	227,791	179,395
Discounts and rebates	<b>719</b>	945	626
Returns	<b>600</b>	791	1,200
Total discounts, rebates and returns	<b>1,319</b>	1,736	1,826
<b>Product sales, net</b>	<b>304,439</b>	<b>226,055</b>	<b>177,569</b>

### Discounts and rebates

Discounts include prompt payment discounts and charge backs. In 2009, our discounts and rebates amounted to € 719 (2008: € 945).

We generally offer our US wholesalers a prompt-pay cash discount as an incentive to remit payment in full within one month after the date of an invoice. Prompt-pay discount calculations are based on the gross amount of each invoice. We account for these discounts by reducing product sales by the estimated discount amount when the product is sold.

Wholesaler charge backs, customary in our industry, are arrangements that relate to contractual agreements to sell products to Group Purchasing Organizations (GPOs) in the US at fixed prices that are lower than the list prices we charge wholesalers. When the GPOs purchase our products through wholesalers at these reduced prices, the wholesaler charges

## Operating and financial review and prospects continued

us for the difference between the price the wholesaler paid to us and the price at which they sold the products to the GPO. Accruals for wholesaler charge backs closely approximate actual results because charge back amounts are fixed at the date of purchase by the GPOs. As the charge backs are settled within a short time of incurring the liability, the outstanding accruals are relatively low.

We offer rebates primarily in connection with attainment of sales targets by wholesalers and large retailers in contractually agreed percentages. The rebates are accrued as the underlying sales transactions are recognized and are based on reasonable estimates on the attainment of the sales targets.

### Returns

Returns that reduce our gross product revenue may arise from the following:

- Customers return of products defective upon delivery;
- Specific right of return in accordance with contractual terms; and
- Returns via the normal distribution channels if the product is in good condition, pursuant to local law in certain jurisdictions.

The Company normally does not accept returns of non-defective product in the form of an exchange but generally issues a cash refund or a credit instead.

In 2009, returns amounted to € 600 (2008: € 791) or approximately 0.2% (2008: 0.4%) of our net product sales.

The following table shows the percentage of products returned as a percentage of the gross product sales per country during 2009 based on the country from which the products were originally sold.

Country	Returns 2009	Returns 2008	Returns 2007
Spain	<b>1.7%</b>	3.0%	2.5%
Italy	<b>0.1%</b>	1.1%	1.4%
Switzerland	<b>0.0%</b>	0.1%	0.1%
US	<b>5.4%</b>	2.1%	1.9%
Sweden	<b>0.1%</b>	0.1%	0.1%
Korea	<b>0.1%</b>	—	—
UK	<b>0.0%</b>	—	—
Netherlands	—	—	—

## Roll-forward information

The table below shows the roll-forward information of our discounts, rebates, and product returns:

In thousands of Euro

	Accrual for discounts and rebates	Provision for returns	Total
<b>January 1, 2009</b>	<b>(189)</b>	<b>(675)</b>	<b>(864)</b>
Additions – current period	(733)	(924)	(1,657)
Actual returns/ credits – current period	710	205	915
Actual returns/ credits – prior period	15	464	479
Release of accruals – current period	14	–	14
Release of accruals – prior period	–	324	324
Effect of movements in exchange rates	(1)	17	16
<b>December 31, 2009</b>	<b>(184)</b>	<b>(589)</b>	<b>(773)</b>

## Discounts and rebates

We base our estimates for discounts and rebates primarily on historical experience and contractual agreements, supplemented by management’s judgment. In 2009, our estimates for rebates based on historical experience did not differ materially from actual results. With respect to discounts, we have limited uncertainties in determining our estimates, because these deductions generally occur within a short time frame of incurring the liability.

For calculating our rebates estimates we make use of quantifiable contractual rebates data. In general, our rebates are based on fixed rebate percentages on product sales to customers that have been granted rebates.

## Returns

We base our estimates of product returns on the percentage of returns that we have experienced historically. We may adjust these return estimates if we are aware of other factors that we believe could meaningfully impact our expected return percentages. For example, in respect of our influenza vaccine, we specifically take into account the development of the flu season, in particular, the number and impact of outbreaks. While we do not have a formula that estimates the impact of the number and impact of outbreaks on the level of the accrual for returned vaccines, an increased number of outbreaks will generally result in a lower accrual for returned influenza vaccines, because it becomes more unlikely that vaccines will be returned. Alternatively, a lower number of outbreaks can result in a higher accrual, because it becomes more likely that influenza vaccines will be returned unused at the end of a mild flu season.

In addition, in our estimates of returns, we take into account other information, such as media coverage of vaccination programs, estimates of inventory levels of our product in the distribution channel, vaccine shelf life and known sales and market trends. These are reflected in the accruals by means of management’s judgment.

Increased media coverage of vaccination programs, either by advertising campaigns or coverage of flu outbreaks, results in an increased public awareness. Consequently, this may lead to an increased number of flu vaccinations and fewer unsold doses with our customers, which limits the level of accruals for product returns.

Relatively high levels of inventory of our product in the distribution channel and short shelf life of product sold can be indicators for an increased level of returns.

## Operating and financial review and prospects continued

Sales and market trends are taken into account by reference to the life cycle phase of products. If product sales show a decreasing revenue pattern over time, this can be an indicator of an increased level of returns. We do not rely on quantitative externally sourced information in our calculation of returns estimates. We are not aware of any available external quantitative information or other quantifiable data that would provide us the benefit of a more reliable estimate.

The rate of product returns is quantifiable. We monitor returns primarily on a per country basis based on the country from which the product was sold because our accruals are determined at this level. Within the individual countries, we monitor the returns on a product-by-product basis. In 2009, our estimates for returns did not differ materially from actual results.

### Tabular disclosure of contractual obligations

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See note 5.24 'Financial instruments – Maturity analysis contractual undiscounted cash flows' in the financial statements for the tabular disclosure of contractual obligations.

### Off-balance sheet arrangements

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As of December 31, 2009, we have no unconsolidated special purpose financing or partnership entities or other off-balance sheet arrangements that have or are reasonably likely to have a current or future effect on our financial condition or lead to changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources, that is material to investors.

The Group has investments in one associate and in one joint venture that are both non-consolidated companies. Details are provided in note 5.9 'Investments in associate and joint venture' in the financial statements.

Further details on our off-balance sheet arrangements such as our guarantees and covenants are disclosed in note 3 'Financial risk management' and note 5.26 'guarantees' in our financial statements.

### Quantitative and qualitative disclosure about market risk

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Market risk is the risk of loss related to adverse changes in market prices, including currency risk, interest rate risk and risk of financial instruments. During the ordinary course of business, the Group is exposed to various financial market risks, primarily from foreign exchange, interest rates and credit risk. Details on our market risks are disclosed in note 3 'Financial risk management' in the financial statements.

### Impact of inflation

Crucell does not operate subsidiaries in countries with hyperinflation. Sales to customers in hyperinflationary countries are made in hard currency, mainly Euro, US Dollar, Swiss Franc and Swedish Crown.

# Corporate governance

## Corporate governance at Crucell

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Corporate governance concerns the relationship between management and the shareholders, and more generally the stakeholders, of the Company. It is the formal codification of the manner in which the Company is governed, of the accountability of its management and its supervision, of the manner in which stakeholders, and more particularly shareholders, are able to gain an insight into the state of affairs within the Company, and finally, of the way in which they can influence the decision-making process. With regard to this final issue, voting rights and the manner in which votes can be exercised, play an important role.

As a Dutch corporation, Crucell is subject to the Dutch Corporate Governance Code (the 'Code'). As a foreign private issuer whose ADSs trade on NASDAQ Global Select Market (NASDAQ), we are also subject to US securities laws (including the provisions of the Sarbanes-Oxley Act of 2002) and the NASDAQ rules.

As a foreign private issuer Crucell may follow its home country practice in lieu of the requirements of certain rules of NASDAQ. Our Annual Report discloses those requirements that are not followed and describes the home country practice that is followed instead, see 'Exemptions from certain NASDAQ Corporate Governance Rules' in this section.

Also under the rules of the SWX Swiss Exchange, where Crucell has a secondary listing, it is allowed to apply the Dutch Corporate Governance Code.

## Corporate governance developments

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We monitor and assess applicable corporate governance rules, including recommendations and initiatives regarding principles of corporate governance. These include those that have been developed in the US, both by NASDAQ and by the SEC pursuant to the Sarbanes-Oxley Act of 2002, as well as in the Netherlands, through the revised Dutch Corporate Governance Code, which came into effect as of the financial year starting on or after January 1, 2009.

## Dutch Corporate Governance Code

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The Code has been instituted by government decree. According to Dutch law, a public company should include in its annual report a statement about the compliance with the principles and best practice provisions of the Code that regard the Management Board and Supervisory Board. If a corporation does not, or does not intend to comply with one or more of the principles and best practice provisions, it must explain its motivation in the annual report. According to the Code, substantial amendments to the Company's existing corporate governance structure and compliance with the Code should be submitted for discussion to the General Meeting of Shareholders.

On December 10, 2008, the Dutch Corporate Governance Code Monitoring Committee (the Monitoring Committee) published the revised Code. This Code amends the original Code and brings it in line with recent corporate governance developments. The revised Code entered into force with effect from the financial year starting on or after January 1, 2009 and can be found at [www.corpgov.nl](http://www.corpgov.nl). The Monitoring Committee recommends that listed companies include a chapter in their annual report 2009 on the broad outline of their corporate governance structure and compliance with the revised Code and present this chapter to the general meeting in 2010 for discussion in a separate agenda item.

Important principles of the Code are:

- Strengthening the role of the Supervisory Board and its committees and increasing its independence, quality and expertise;
- Strengthening the role of the shareholders with respect to control of the functioning of the Management Board and the Supervisory Board, as well as with respect to nomination and remuneration of members of the Management Board and the Supervisory Board;
- Facilitating and stimulating shareholders to use their voting power and to actively participate in the General Meeting of Shareholders;



## Corporate governance continued

- Defining the role of the external auditor vis-à-vis the Supervisory Board as its principal contact; and
- Maintaining an appropriate internal risk and control system.

For an overview of Crucell's conformity with the Code, please refer to our website ([www.crucell.com](http://www.crucell.com)), where the following documents can be consulted:

- By-laws of the Management Board;
- Remuneration policy Management Board;
- By-laws of the Supervisory Board; and
- Code of Conduct (Crucell's company code) including whistle-blower policy.

We have adopted a code of business conduct and ethics (Code of Conduct) that applies to all employees of the Company, including our principal executive officer and principal financial officer, and reflects that we are a fully integrated company that operates in numerous countries. The Code of Conduct underlines that one of the most valuable assets of Crucell is its integrity. No waivers of the Code of Conduct were granted during 2009.

We have a whistle blower policy in place, which encourages employees to report abuses and non-compliance with our Code of Conduct, anonymously if necessary.

### Compliance with the Code

In June 2005, the General Meeting of Shareholders approved our current corporate governance structure. Except for the four provisions of the Code referenced below Crucell has fully implemented the recommendations set forth in the Code and incorporated them into its corporate governance policies.

### Exceptions to compliance with the Code

The Code contains a 'comply-or-explain' principle, offering the possibility to deviate from the Code as long as any such deviations are explained. Crucell complies with all of the principles and best practice provisions of the Code, except for the following:

### Remuneration of Management Board members

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Under the Code, the maximum severance pay for a Management Board member should be no more than one year's salary, unless this is manifestly unreasonable. We do not apply this principle in the event of a dismissal arising from an unwanted change of control for Management Board members. The employment contracts of those members of the Management Board that were already in place as at 1 January 2004 (the date on which the Code took effect) remain unchanged. In other cases, agreed severance payments can be higher than one year's salary if otherwise this would obstruct the recruitment of the right person for a Management Board position.

### Loans to the Company's management

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We do not apply the provision in the Code that no personal loans shall be granted to a company's Management Board member because, prior to the Code's development and passage of similar legislation in the US, loans were made to Management Board members and one such loan currently remains outstanding. Reference is made to the Remuneration report in this section. We have not granted additional loans to Management Board members since 2002.

### Claw Back of Variable Remuneration

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We do not apply the provision in the Code that the Supervisory Board may recover from the Management Board members any variable remuneration awarded on the basis of incorrect financial or other data (claw back clause). In 2010, the supervisory board of Crucell will investigate the possibility to implement such a claw back clause.

### Remuneration of Supervisory Board members

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We do not apply the provision that remuneration of the members of the Supervisory Board should not include share grants. Crucell deems this form of remuneration adequate because this is customary among biotechnology companies operating internationally, and it helps attract well-qualified

supervisory directors with specific expertise in biotechnology and international business fields.

### **Exemptions from certain NASDAQ corporate governance rules**

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NASDAQ rules provide that NASDAQ may provide exemptions from the NASDAQ corporate governance standards to a foreign issuer when those standards are contrary to a law, rule or regulation of any public authority exercising jurisdiction over such issuer or contrary to generally accepted business practices in the issuer's country of domicile. We are exempt from certain NASDAQ corporate governance standards that are contrary to the laws, rules, regulations or generally accepted business practices of the Netherlands. These exemptions and the practices followed by our Company are described below:

- We are exempt from NASDAQ's quorum requirements applicable to meetings of shareholders. In keeping with Dutch law and generally accepted business practice, our articles of association provide that there are no quorum requirements for the General Meeting of Shareholders.
- We are exempt from NASDAQ's requirements regarding the solicitation of proxies and provision of proxy statements for meetings of shareholders. We inform shareholders of meetings in a public notice, but we do not solicit proxies for the General Meeting of Shareholders. Dutch law does not have a regulatory regime for the solicitation of proxies and the solicitation of proxies is not a generally accepted business practice in the Netherlands. In connection with our American Depositary Shares (ADSs), the Bank of New York Mellon, as depositary, distributes proxy materials to holders of our ADSs.
- NASDAQ requires shareholder approval prior to the issuance of securities when a stock option or purchase plan is to be established or materially amended or other equity compensation arrangement made or materially amended, pursuant to which stock may be acquired by officers, directors, employees, or consultants. Under Dutch Company law and the Code shareholder approval is only required for equity compensation plans (or changes thereto) for members of the Management Board and Supervisory Board, and not for equity compensation plans for other groups of employees. Our articles of association provide that a resolution of the General Meeting of Shareholders to amend our articles of association, to dissolve the Company, or to merge or demerge the Company shall only be adopted on a proposal of the Supervisory Board.
- We do not distribute Annual Reports to all of our shareholders in accordance with NASDAQ rules. As our shares are bearer shares, according to Dutch law we are not required to distribute copies of annual and interim reports to all shareholders. Copies of such reports are available to shareholders at our corporate headquarters, and are filed with NASDAQ and the Bank of New York Mellon as depositary under our depositary agreement relating to our ADSs. Upon request the Bank of New York Mellon distributes our Annual Reports to holders of our ADSs.
- The Company has a two-tiered board structure, in contrast to the one-tier board structure used by most US companies. In the Netherlands, a public limited liability company has a Management Board as its management body and a Supervisory Board which advises and supervises the Management Board. In general, Management Board members are employees of the company while members of the Supervisory Board are often former state or business leaders and sometimes former members of the Management Board. Members of the Management Board and other officers and employees cannot simultaneously act as members of the Supervisory Board. The Supervisory Board must approve certain specified decisions of the Management Board. Under the Code all members of the Supervisory Board with the exception of not more than one person, shall be 'independent'. The definition of 'independence' under the Code however, differs from the definition of 'independence' under the NASDAQ listing standards (e.g. employment by the Company in the three years prior to the appointment as member of the Supervisory Board versus five years under NASDAQ and the Code respectively).
- Dutch law requires that the external auditors be appointed at the General Meeting of Shareholders and not by the Audit Committee.

### **Directors, senior management and board practices**

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Crucell has a 'two-tier' governance structure, in which executive and supervisory responsibilities are clearly segregated. Our Management Board is responsible for managing the Company's daily affairs and business and, as such, is responsible for achieving Crucell's goals, strategy, policy, and results.

## Corporate governance continued

### Supervisory Board

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The Supervisory Board, which consists solely of independent directors, supervises the Management Board. In the execution of their duties, the members of the Supervisory Board must be guided by the best interests of Crucell and its stakeholders.

The Supervisory Board reports to the General Meeting of Shareholders with regard to the corporate governance of Crucell, its structure and the compliance with applicable internal and external rules and regulations.

The principal duty of the Supervisory Board is to supervise the policies of the Management Board and to provide advice. The Supervisory Board oversees the corporate strategy, the risks inherent in the Company's activities and supervises the structure and operation of the internal risk management and control systems, the financial reporting process and the Company's compliance with relevant legislation and regulations.

Our Supervisory Board must approve certain categories of resolutions of our Management Board, which categories are specified in our articles of association. In addition, our Supervisory Board may give our Management Board written notice of other corporate actions that it wishes to approve. The division of duties and the procedures within the Supervisory Board are set forth in the by-laws of the Supervisory Board and can be found on Crucell's website ([www.crucell.com](http://www.crucell.com)).

Our articles of association provide that at least three Supervisory Board members must serve on our Supervisory Board. We must fill any vacancies on the Supervisory Board as soon as possible, but until they are filled, the remaining members of our Supervisory Board constitute a competent board. Under Dutch law, Supervisory Board members cannot serve as members of our Management Board.

The members of our Supervisory Board are appointed for terms ending on the date of the first General Meeting of Shareholders that is held four years after the date of their appointment. They may be reappointed for two additional consecutive terms of four years each. Our Supervisory Board nominates its own members and aims for an international and adequate composition reflecting the global activities of Crucell, as well as for an adequate level of experience in financial, economic, medical, scientific, technological, social and legal aspects of international business. To be binding, there must be at least two nominees for each vacancy on the Supervisory Board. The nominee earning the highest number of votes of Supervisory Board members becomes a binding nomination. The General Meeting of Shareholders can override these binding nominations by a vote of an absolute majority of the votes cast. This vote must represent more than one third of our total issued and outstanding share capital. If the Supervisory Board does not make any nominations within three months after a vacancy has occurred, our General Meeting of Shareholders can fill Supervisory Board vacancies. If the Supervisory Board makes a non-binding nomination (i.e., only one nominee is presented to the Supervisory Board for any particular vacancy), then such nomination can only be overturned by a resolution of the General Meeting of Shareholders taken by an absolute majority of the votes cast, representing at least one third of the Company's total issued and outstanding share capital. The Supervisory Board members retire according to a rotation plan established by the Supervisory Board itself.

A Supervisory Board member can be suspended or dismissed at any time by a resolution of a General Meeting of Shareholders passed by an absolute majority of the votes cast. This vote must represent more than one third of our total issued and outstanding share capital if the resolution to suspend or dismiss a Supervisory Board member is not proposed by the Supervisory Board itself. Within three months after a suspension, a General Meeting of Shareholders must either dismiss the Supervisory Board member, terminate or extend the suspension. The total suspension may not exceed three months.

Our Supervisory Board appoints its own chairman and vice-chairman. The chairman of the Supervisory Board is primarily responsible for the functioning of the Supervisory Board and its committees. He acts as the spokesman of the Supervisory Board and is the main contact for the CEO and the Management Board as a whole. The CEO and the chairman of the Supervisory Board meet on a regular basis. As a general rule, the chairman of the Supervisory Board presides over General Meetings of Shareholders. The vice-chairman replaces, and assumes the powers and duties of, the chairman in the latter's absence.

The Supervisory Board must adopt rules for its own internal governance, including the creation of committees. The Supervisory Board must, in any event, establish an Audit Committee, a Remuneration Committee and a Nomination Committee. Passing Supervisory Board decisions requires a majority of the votes cast at a meeting of our Supervisory Board, unless otherwise provided for in the articles of association or the by-laws of the Supervisory Board. The Company Secretary assists the Supervisory Board.

The General Meeting of Shareholders determines the Supervisory Board members' compensation. We pay our Supervisory Board members in ordinary shares and cash, or cash only, at the member's discretion. We also reimburse Supervisory Board members for their expenses incurred in work relating to Crucell. The remuneration policy is intended to be able to attract and retain qualified and expert Supervisory Board members. It is in line with what is customary in the US biotechnology industry and is in line, as much as possible, with the best practice provisions of the Code.

According to the best practice provisions of the Code, an individual may hold a maximum of five Supervisory Board memberships in Dutch listed companies, with the chairmanship of a Supervisory Board counting as two memberships. All members of our Supervisory Board comply with this provision.

All members of the Supervisory Board comply with the criteria for independence as set out in the NASDAQ rules, the Code and the requirements of applicable EU and Swiss rules.

The business address of each Supervisory Board member is the address of our principal executive office in Leiden, the Netherlands.

## **2009 Supervisory Board activities**

The Supervisory Board held thirteen meetings with the Management Board in 2009, of which eight were in the form of conference calls. The meetings were arranged in such a way that, on several occasions, the Supervisory Board could meet immediately after the departure of the Management Board; so called closed sessions. There were also a number of more informal contacts between Supervisory Board Members and the Management Board.

The Supervisory Board was closely involved in all developments affecting the Company in terms of strategy, tactics and operations in the financial year 2009. The Board's meeting schedule not only reflects its commitment to the Company's affairs, but also to the dynamic way in which the Company is rapidly consolidating its position in the biotech industry. Thanks to the well-documented information provided by, and to, the frequent discussions with the Management Board, the Supervisory Board was able to acquire a comprehensive perspective on all aspects of the Company's strategy. Where Supervisory Board approval of proposals was required, it was able to arrive at decisions based on solid facts and coherent arguments.

All Supervisory Board meetings and conference calls were well attended. Regular items on the agenda included the Company's financial performance, based on quarterly reports, its budget and its business, including the research & development portfolio, intellectual property matters and operational updates. Importantly the Board also discussed the Company's strategy and its near-, mid- and long-term risks, the current and future strategic objectives, planned acquisitions, the JNJ strategic collaboration, sanofi pasteur and DSM collaborations and the reports from the Audit Committee, the Remuneration Committee, Research & Development Committee and Nomination Committee. Other significant issues addressed were compliance with Section 404 of the American Sarbanes-Oxley Act of 2002 and related regulations (SOX 404), the ongoing corporate rationalization processes and the progress made in integrating acquired businesses.

The Supervisory Board also discussed its own performance, reviewing its function and its individual members; and the performance of the Management Board and its individual members. The design of the strategic collaboration between Crucell and JNJ was discussed frequently and in detail with the Management Board and its financial advisors. In particular, the legal and financial consequences of such

## Corporate governance continued

strategic collaboration were reviewed with Crucell's in-house and outside legal advisors.

### Composition Supervisory Board

As of December 31, 2009 the Supervisory Board of Crucell consisted of:

Name	Age	Position	End of current term
Jan Oosterveld	65	Chairman	2010
Phillip Satow	68	Member	2013
Claes Wilhelmsson	70	Member	2011
Seán Lance	62	Vice-Chairman	2011
Arnold Hoevenaars	60	Member	2013
Steve Davis	52	Member	2012
Floris Waller <sup>1</sup>	51	Member	2013

<sup>1</sup> Mr. Waller was appointed as member of the Supervisory Board at the Company's General Meeting of Shareholders on June 5, 2009.

**Mr. Jan Oosterveld** has served as chairman of our Supervisory Board since June 2006 and as a member of the Supervisory Board since his appointment at the General Meeting of Shareholders on June 3, 2004. In 2004 he retired as a member of the Group Management Committee from Royal Philips Electronics N.V. after an international career of 32 years. At his retirement he was in charge of Corporate Strategy, Alliances, Restructuring and Redesign and the regional organizations; he was also the CEO of Philips Asia Pacific. In addition, he was the Chairman of the board of LG. Philips, a 50-50 joint venture between LGE and Philips, at the time the world's largest LCD company. He holds a masters degree in mechanical engineering from the Technical University Eindhoven and an MBA from the Instituto de Estudios Superiores de la Empresa (IESE) in Barcelona. He became a professor at IESE in 2004. Mr. Oosterveld is a member of the Board of Barco, Belgium; Cookson Group, U.K.; and Candover Investments, U.K. He is also a member of the Supervisory Board of the University of Groningen and the Chancellor of the International Academy of Management. Mr. Oosterveld is a Dutch citizen.

**Mr. Phillip Satow** has served as a member of our Supervisory Board since our incorporation. He worked 14 years with Pfizer, Inc. where his last position was Vice President, Pfizer Europe. From 1985 to 1997, he was Executive Vice President Marketing at Forest Laboratories, Inc. From 1998 to 1999 he was President of Forest Pharmaceuticals, and Executive Vice President of Forest Laboratories Inc. In addition to the Forest Laboratories board, which he served on from 1999 to 2005, Mr. Satow is a former board member of Eyetech Pharmaceuticals Inc. and Noven Pharmaceuticals Inc. Mr Satow also co founded and served as Chairman and CEO of JDS Pharmaceuticals LLC, a privately held company that was sold to Noven Pharmaceuticals Inc. in 2007. Mr Satow is a US citizen.

**Mr. Claes Wilhelmsson** has served as a member of our Supervisory Board since May 2003. He was previously the Executive Director of Research and Development of AstraZeneca plc from 1999 to July 2002, responsible for AstraZeneca's global R&D. He joined Astra in 1985 and held various positions until the company merged with Zeneca in 1999. Prior to working for Astra, he was a lecturer and researcher at the University of Göteborg in Sweden, where he also completed his medical education and PhD. He currently serves on the boards of a number of biotechnology and start-up companies. Dr. Wilhelmsson previously served on the board of AstraZeneca plc. Mr. Wilhelmsson is a Swedish citizen.

**Mr. Seán Lance** has served as a member of our Supervisory Board since January 2004. Mr. Lance is a former Chairman of Chiron Corporation. He joined Chiron as President and Chief Executive Officer in 1998. From 1985 to 1998 he was employed at Glaxo Holdings where his last position was group Chief Operating Officer and CEO designate. He is a former President of the International Federation of Pharmaceutical Manufacturers Association. Mr. Lance is a chartered company secretary and administrator and also holds a post-graduate degree in Advanced Financial Management. Mr. Lance is a South African citizen.

**Mr. Arnold Hoevenaars** has served as a member of our Supervisory Board since June 2005. Mr. Hoevenaars is a chartered accountant in the Netherlands and his previous positions include, among others, Chairman of the Management Board of the Achmea Group; Chairman of the Board of Directors and Chairman/CEO of the Executive Board of Eureko B.V.; and Member of the Management Board and CFO of Royal Boskalis Westminster N.V. Currently Mr. Hoevenaars serves on several Supervisory Boards of companies and cultural, educational and social welfare institutions. He also is a consultant to several companies. Mr. Hoevenaars is a Dutch citizen.

**Mr. Steve Davis** has served as a member of our Supervisory Board since June 2008. Mr. Davis is a Senior Advisor to McKinsey & Company's Social Sector Office based in Seattle, Washington, US. He is also a Senior Fellow in Intellectual Property at the University of Washington School of Law. He recently served as the interim CEO of the Infectious Disease Research Institute (IDRI). Previously, Mr. Davis was CEO of Corbis Corporation, a global digital media company. He has held positions with the United Nations High Commission for Refugees and several refugee resettlement programs. Currently, he is a member of the Board of Trustees for PATH, a non-profit organization focused on improving public health in the developing world, and the Fred Hutchinson Cancer Research Center, one of the world's leading cancer centers, where he is Vice-Chair. He also holds board positions with The Seattle Foundation and Global Partnerships, and is a member of the Council on Foreign Relations. Mr. Davis holds a Bachelor of Arts from Princeton University, a Master of Arts from the University of Washington and a Doctorate in Law from Columbia University School of Law. Mr. Davis is a US citizen.

**Mr. Floris Waller** was appointed as a member of our Supervisory Board at the annual general meeting of shareholders on June 5, 2009. He was CFO and board member at Corporate Express N.V. (previously Buhrmann) from 1999 until 2008. Mr. Waller was a member of the Supervisory Board and Audit Committee of Univar N.V. from 2005 until 2007. From 1984 until 1999, Mr. Waller held various senior finance and operational positions at Unilever N.V./Plc. Currently he is CFO and board member of Pon Holdings B.V. and is a member of the Supervisory Board of Klaverblad, a local insurance company in the Netherlands. Mr. Waller holds a Master of Science degree in Business Economics from Erasmus Universiteit of Rotterdam and is a chartered accountant. Mr. Waller is a Dutch citizen.

## Committees

The Supervisory Board appoints from its members an Audit Committee, a Remuneration Committee, a Nomination Committee and a Scientific Advisory Committee. The function of these committees is to advise and assist the Supervisory Board to make decisions.

### Audit Committee

Arnold Hoevenaars (chairman), Seán Lance and Floris Waller.

In 2009, the Audit Committee met nine times, of which four were conference calls. The Audit Committee currently consists of three Supervisory Board members who are independent within the meaning of the NASDAQ listing rules and the Code. The Audit Committee is responsible for, among other things, reviewing our annual and interim reports and accounts, for securing and monitoring our external auditors' involvement in that process, and supervising the internal control system and internal audit function. The Audit Committee is the first point of contact of the external auditor when irregularities are found in the contents of the financial reports. Ultimate responsibility for reviewing our Annual Report and interim financial reporting lies with our Supervisory Board. At the request of the Audit Committee, the chairman of the Supervisory Board may be invited to attend its meetings.

Our Audit Committee is in compliance with all of the relevant rules and regulations of the Netherlands. We believe that the members of our Audit Committee have sufficient financial and other experience to perform their responsibilities on the Committee. Mr. A. Hoevenaars is a 'financial expert' as defined in the rules promulgated under the Sarbanes-Oxley Act of 2002.

### Remuneration Committee

Phillip Satow (chairman), Claes Wilhelmsson and Jan Oosterveld. Mr. Satow meets the requirements as outlined in best practice provision III. 5.1.1 of The Dutch Corporate Governance Code.

In 2009, the remuneration Committee met four times.

The Remuneration Committee advises on policies and reviews and determines objectives relevant to the compensation of the members of the Management Board and members of the Management Committee. The Remuneration Committee evaluates the performance of members of the Management



## Corporate governance continued

Board and Management Committee in view of these objectives and advises on the compensation of the members. In advising on short and long-term incentive compensation, the Remuneration Committee considers, among other factors, our financial and commercial performance, scientific performance and progress and any increases in the value of the Company. External compensation survey data available for the biotechnology industry is also used as a benchmark for determining compensation levels. It is the aim of the Remuneration Committee to position the remuneration packages for members of the Management Board and Management Committee at competitive levels. Bonuses are paid to members of the Management Board in connection with achievement of certain objectives set by the Supervisory Board.

Crucell maintains stock option plans whereby the Remuneration Committee may grant options to employees and members of the Management Board and Supervisory Board as well as non-employees in exchange for consulting services, subject to approval by the shareholders.

In addition, the Remuneration Committee reviews the general compensation and benefit policies for all of our employees.

The Supervisory Board of Crucell has been assisted by an independent external remuneration consultant. The Remuneration Committee ensures that the consultant reporting to the Supervisory Board acts independently from the Company and does not provide advice to members of the Management Board or Management Committee.

### **Nomination Committee**

The Nomination Committee consists of all of the Supervisory Board members and as such met four times in 2009. This committee (a) draws up selection criteria and appointment procedures for members of the Supervisory Board and the Management Board, (b) periodically assesses the size and composition of the Supervisory Board and the Management Board and makes proposals of nominees to the Supervisory Board, (c) periodically assesses the functioning of individual members of the Supervisory Board and the

Management Board, and reports on this to the Supervisory Board and (d) supervises the policy of the Management Board on the selection criteria and appointment procedures for senior management. The committee also makes proposals for appointments of Management Board members to the Supervisory Board.

### **Scientific Advisory Committee**

Claes Wilhelmsson (chairman), Steve Davis

This committee is responsible for, among other things, reviewing progress in our research and development activities. The committee held two meetings with R&D management to discuss issues around protein production and various infectious diseases. They also covered R&D budgets and organizational matters. The committee reports to the Supervisory Board on a regular basis.

### **Management Board**

Our Management Board manages our general affairs and business, under the supervision of our Supervisory Board. Under our articles of association, the Management Board requires prior approval of the Supervisory Board to:

- Expand into a new, or cease an existing, line of business;
- Participate, sell an interest, change its participation, or otherwise take an interest in, or assume the management of, another business enterprise;
- Enter into, terminate or amend any joint venture or pooling arrangement;
- Acquire fixed assets exceeding price limits set by the Supervisory Board; and
- Enter into financial commitments, other than in the ordinary course of business and/or exceeding price limits set by the Supervisory Board or for longer than a year.

Under Dutch law, in certain circumstances, Management Board actions may require the approval of the General Meeting of Shareholders.

Our Supervisory Board determines the size of our Management Board after consultation with our Chief Executive Officer. The General Meeting of Shareholders appoints the members of our Management Board from a list of candidates nominated by our Supervisory Board. If the list of members contains the names of at least two persons it shall be binding. However, the general meeting of shareholders may at any time, by resolution passed with an absolute majority of the votes cast representing more than one third of the Company's issued capital, resolve that such list shall not be binding. If our Supervisory Board does not nominate anyone for a specific position within three months after a vacancy occurs, our General Meeting of Shareholders can appoint a member at its own discretion. If the Supervisory Board makes a non-binding nomination (i.e., only one nominee is presented to the Supervisory Board for any particular vacancy), then such nomination can only be overturned by a resolution of the General Meeting of Shareholders taken by an absolute majority of the votes cast, representing at least one third of the Company's total issued and outstanding share capital. A member of the Management Board may be appointed or reappointed for a term of not more than four years at a time.

Our Management Board may establish rules governing its internal organization. Our Supervisory Board must approve the adoption of and any changes to these rules. Our Management Board may charge each member of the Management Board with particular duties. The allocation of duties requires the approval of the Supervisory Board. Resolutions of our Management Board are passed by a majority of votes cast, unless provided otherwise in the by-laws of the Management Board. The Management Board shall appoint a Company Secretary who will assist the Management Board. The appointment and dismissal of the Company Secretary requires the approval of the Supervisory Board.

Each member of the Management Board may be suspended or removed by the General Meeting of Shareholders at any time. A resolution to suspend, remove or revoke the suspension of a member of the Management Board other than at the proposal of the Supervisory Board may only be passed by the General Meeting of Shareholders with an absolute majority of the votes cast representing at least one third of the Company's total issued and outstanding share capital.

Our Supervisory Board may also suspend (but not dismiss) a member of our Management Board. We must hold a General Meeting of Shareholders within three months after a suspension to either terminate or extend it. Any suspension may be extended one or more times, but may not last longer than three months in the aggregate. If at the end of that period no decision has been taken on termination of the suspension, or on removal, the suspension shall cease.

Our Supervisory Board determines the compensation and benefits of the members of our Management Board, based on a proposal by the Remuneration Committee, within the scope of the remuneration policy adopted by the General Meeting of Shareholders. The business address of the members of our Management Board is the same as the address of our principal executive office in Leiden, the Netherlands.

Pursuant to the Code, members of the Management Board are allowed to hold a maximum of two Supervisory Board positions in other listed companies.

The name, date of appointment and position of the members of our Management Board are:

Name/Position	Date of appointment
Ronald Brus Chairman of the Management Board, President and Chief Executive Officer	May 30, 2008
Leonard Kruimer Chief Financial Officer	May 30, 2008
Cees de Jong Chief Financial Officer	May 30, 2008
Jaap Goudsmit Chief Scientific Officer	May 30, 2008

### **Management Committee**

For its day-to-day operations Crucell has established a Management Committee that is responsible for the design, implementation and management of long and short-term strategy under the ultimate responsibility of the Management Board. The Management Board determines the number of members of the Management Committee. Members of the Management Committee are appointed and dismissed by the Management Board, with the approval of our Supervisory Board. The Management Committee generally meets once a month, and works closely with other members of our management. Our Management Board may establish rules governing its relationship with our Management Committee. Our Supervisory Board must approve the adoption of and any changes to these rules.

## Corporate governance continued

The following table sets forth the name, age and position of each of the members of our Management Committee:

Name/position	Age
Ronald Brus Chairman of Management Committee, President and Chief Executive Officer	46
Leonard Kruimer Chief Financial Officer	51
Cees de Jong Chief Operating Officer	48
Jaap Goudsmit Chief Scientific Officer	58
René Beukema General Counsel and Corporate Secretary	45
Arthur Lahr Chief Strategy Officer & Executive Vice President Business Development	41

The following paragraphs contain brief biographies of the members of our Management Board and the members of our Management Committee:

**Mr. Ronald Brus** is chairman of the Management Board and President and Chief Executive Officer since January 2004, and has been a member of our Management Committee since incorporation. He was Executive Vice President, Business Development at IntroGene from 1997 to 2000 and Chief Operating Officer at Crucell from March 2003 until his appointment as President and Chief Executive Officer. From 1994 to 1996, he was product-planning physician at Forest Laboratories (New York) and from 1990 to 1994 he was medical director for Zambon B.V. He holds a medical degree (MD) from the University of Groningen. Mr. Brus is a Dutch citizen.

**Mr. Leonard Kruimer** became a member of the Management Board in January 2005. He has been our Chief Financial Officer and a member of our Management Committee since incorporation. He held the same position at IntroGene from 1998 to 2000. From 1996 to 1998 he was an independent consultant with companies such as Pepsico and Royal Boskalis Westminster N.V. From 1988 to 1995, he held senior executive positions at Continental Can Europe, GE Capital/TIP Europe and Kwik-Fit Europe B.V. He was a consultant at

McKinsey & Co. and has worked with Price Waterhouse & Co. He holds a Masters in Business Administration from the Harvard Business School, a degree from the University of Massachusetts, Amherst, and is a CPA in New York State. Mr. Kruimer is a Dutch citizen.

**Mr. Cees de Jong** joined Crucell as Chief Operating Officer in 2007. Prior to joining Crucell Mr. de Jong was with Quest International in Naarden, the Netherlands as a member of the Board and responsible for the Flavours Division Mr. de Jong has also worked as Managing Director of DSM Anti-infectives. In 1989 Mr. de Jong started his career at Gist Brocades, holding a variety of roles in business development, strategy and general management before the company's acquisition by DSM in 1998. Mr. de Jong is Chairman of the Supervisory Board of GreenChem Holding International B.V. Mr. de Jong holds a Medical Degree from the Erasmus University of Rotterdam and an MBA from the RSM Erasmus University. Mr. de Jong is a Dutch citizen.

**Mr. Jaap Goudsmit** is a member of the Management Board since January 2004. He was Senior Vice President Vaccine Research from September 2001 until July 2002 and member of the Management Committee from July 2002 as Executive Vice President Vaccine R&D. In September 2002 he was appointed Chief Scientific Officer. He chaired the Academic Medical Center of the University of Amsterdam, the Research Institute for Infectious Diseases and the Institute for Science Education. He was the founding Chairman of the Scientific Advisory Committee of the International AIDS Vaccine Initiative (IAVI) and the founding co-Chairman of the European Vaccine Effort against HIV/AIDS (EuroVac). Since 1989, he has been a professor at the University of Amsterdam and the Academic Medical Center. He holds a medical degree (MD) and a PhD from the University of Amsterdam. Mr. Goudsmit is a Dutch citizen.

**Mr. René Beukema** has been our General Counsel and Company Secretary since our incorporation. He held the same position at IntroGene from 1999 to 2000. From 1994 to 1999 Mr. Beukema was senior legal counsel for GE Capital/TIP Europe. From 1991 to 1994, he was legal counsel for

TNT Express Worldwide N.V. He has a Masters in Law from the University of Amsterdam. Mr. Beukema is a Dutch citizen.

**Mr. Arthur Lahr** is Crucell's Chief Strategy Officer and Executive Vice President Business Development. He joined Crucell in April 2001 as Executive Director Business Development, was appointed Vice President Business Development in December 2003, a member of the Management Committee in January 2004; Executive Vice President in January 2006; and assumed responsibility for European marketing and sales and company strategy in 2006. From 1994 to 2001, he was a consultant with McKinsey & Co. Prior to that, he worked with Unilever. He holds a Masters in Business Administration from INSEAD and a Masters in Science, Applied Physics, from the University of Delft.

### **Disclosure Committee**

The Disclosure Committee is designed to help senior management, particularly the Chief Executive Officer and Chief Financial Officer, in the maintenance and evaluation of our disclosure controls and procedures. The Disclosure Committee gathers all relevant financial and non-financial information and assesses materiality, timeliness and necessity of disclosure of such information. The Disclosure Committee is comprised of the members of the Management Committee and selected senior managers. Members of the Disclosure Committee have direct access to our external legal counsel and our external auditor. The Disclosure Committee reports to the Chief Executive Officer and Chief Financial Officer.

The Disclosure Committee is an integrated part of our organization and is essential to our internal control over financial reporting. The Disclosure Committee and additional actions taken to further improve disclosure and internal control are intended to help us comply with the requirements of the Sarbanes-Oxley Act of 2002 and regulations promulgated by the Securities and Exchange Commission under that Act.

### **Remuneration report for Management Board and Supervisory Board**

The Remuneration report for Management Board and Supervisory Board contains required disclosures on key management personnel compensation, as meant in IAS 24. These disclosures are deemed to be part of the financial statements, specifically note 5.30 'Related parties – Remuneration report for Management Board and Supervisory Board'.

### **Remuneration structure**

The remuneration policy for the Management Board and Supervisory Board was first adopted by the General Meeting of Shareholders in 2005. An amended version of this remuneration policy was adopted by the General Meeting of Shareholders in 2008. The remuneration policy is based on the following principles:

- Overall remuneration levels need to be sufficient to attract, retain and motivate top management given the dynamic business environment in which Crucell competes for talent;
- Base salaries should be broadly in line with average market levels, whereas short- and long-term incentive levels should reflect an upside potential in case of outstanding performance;
- To enhance the effectiveness of the short-term incentive, clearly measurable and challenging targets are set, which reflect Crucell's strategic focus in the short-term; and
- The long-term incentive plan should ensure a focus on longer-term strategic performance targets, which aim for shareholder alignment and motivation and retention of qualified executives.

The Management Board members receive fixed remuneration in the form of a base salary as well as performance-based compensation in the form of a short-term incentive (STI) plan and a long-term incentive (LTI) plan. Variable pay makes up a substantial part of the pay package, with a large part of variable pay being conditional on meeting targets that are derived from Crucell's long-term strategic agenda.

The structure of the short-term and long-term variable pay elements has been set up in such a way that it contributes to keeping Crucell with its risk profile. This is assured by amongst others:

- Conducting scenario analyses before drawing up the remuneration policy and determining the remuneration of individual Management Board members: the Supervisory Board analyzes the possible outcomes of the variable remuneration components and how they may affect the remuneration of the Management Board members;
- Operating a discretionary authority for the Supervisory Board – the short-term incentive can be adjusted upwards or downwards by 25 percent.

## Corporate governance continued

The STI and LTI plans are described in further detail below. The incentive for achieving target performance for the Chief Executive Officer equals 115% of base salary (65% in short-term incentive and 50% in long-term incentive). For other Management Board members the incentive is 90% of base salary (50% in short-term incentive and 40% in long-term incentive). For the Chief Executive Officer, this breaks down to 46.5% of salary in fixed compensation and 53.5% of salary in performance-based compensation. For the other three Management Board members, the breakdown is 52.6% fixed compensation compared to 47.4% performance-based compensation.

### Management Board service contracts

The contracts for the Management Board members have been entered into for an indefinite period and provide for a notice period of up to six months upon termination by the Company and a notice period of three months upon termination by the individual. Nominations for a seat on the Management Board are for a period of four years.

A dismissal arising from an unwanted change of control will result in a severance arrangement limited to a maximum of two years' worth of base salaries for the Management Board members.

The contracts of the Management Board members contain non-compete provisions that would apply for a period of one year after the end of their employment with us.

### Base salary

The Supervisory Board regularly considers whether base salary levels should be adjusted according to external and internal business factors. In order to ensure that the pay package that is offered to the Management Board of Crucell is competitive, the Supervisory Board has assessed pay levels against a reference market consisting of companies that are comparable in size and complexity (during an assessment that was conducted in 2009, the Supervisory Board has taken account of AMX listed companies).

In 2009, base salary levels for the Management Board were increased by an average of four percent in order to keep up with inflation.

### Short-term incentive

At the General Meeting of Shareholders in 2008, our shareholders approved the implementation of an amended short-term cash-based incentive plan (STI). In the approved policy, payment of the bonus begins upon 70% achievement of certain milestones. In order to compensate higher achievement of certain milestones, the payment limit was increased from 100% to 130%.

The STI bonus is linked to the achievement of predetermined collective and individual milestones. Milestones linked to the STI bonus plan are revised annually and approved by our Supervisory Board.

The collective milestones are based on predetermined annual goals for research, development, business development, finance, intellectual property and corporate legal affairs. Examples of the collective performance measures that have been used during 2009 are amongst others: revenues and profitability. We do not disclose specific targets that have been set as these qualify as commercially sensitive information.

The individual milestones depend on the specific responsibilities of the individual Management Board member and are in most cases derived from the company milestones. Examples of individual performance measures for 2009 were revenues and development milestones.

The table below shows the relative weight of the collective and individual milestones in the STI bonus plan structure:

Management Board	Collective milestones	Individual milestones
CEO, CFO, CSO, COO	70%	30%

The Supervisory Board monitors performance every quarter and measures performance based on both a quantitative (formulaic) approach and qualitative approach (discretionary judgement / test of reasonableness). The type of performance measuring that takes place depends on the specific performance measure. The internal and external auditors are involved to make sure that the agreed-upon procedures for performance measuring and determination of pay out are being followed.

### One-off awards

The Supervisory Board has decided to allocate members of the Management Board and certain other employees a one-off special cash award in recognition of the successful negotiation and closing of the agreement with Johnson and Johnson affiliates, especially in light of the transformational nature of the agreement and the substantial savings of associated transaction costs. In total a cash bonus in thousands of Euro of € 1,206 was paid to members of the Management Board. The cash bonus was allocated as follows: the CEO received € 384 and the other Management Board members each € 274.

### Long-term incentive

Target LTI compensation levels amount to 50% of base salary for the Chief Executive Officer and 40% for the other Management Board members. The LTI compensation can be increased up to 200% of the target award when achieving maximum performance.

Under the terms of the LTI plan, options are conditionally granted and vest at the end of a three-year performance period. The number of LTI options that vests depends on the fulfillment of the LTI performance condition. As a performance condition the total shareholders return (TSR) is compared to the NASDAQ Biotech index after three years of granting the conditional options.

On a vesting date Crucell's Total Shareholder Return (TSR) performance is measured against the performance of the NASDAQ Biotechnology Index during the applicable performance period. The period used to calculate the TSR performance will be the average of the first three months of year one and the average of the last three months of year three. Vesting of the options takes place on January 1 of year four.

The positive difference in percentages, if any, between Crucell's TSR compared to the performance of the NASDAQ Biotechnology Index, determines the number of LTI options which vest, in accordance with the table set out below:

### NASDAQ Biotech Index Vesting Scheme

Positive difference between TSR performance Crucell and the NASDAQ Biotech Index	Vesting as % of target award
≥ 50	200%
≥ 35 and < 50	150%
≥ 20 and < 35	100%
≥ 10 and < 20	50%
≥ 0 and < 10	25%
< 0	0%

At the forthcoming General Meeting of Shareholders the following adjustments to the remuneration policy will be submitted for approval. The target LTI compensation level for the Chief Executive Officer will be increased from 50% of base salary to 65% and for the other Management Board members target LTI compensation levels will be increased from 40% of base salary to 50%.

### Pension

At the beginning of our 2005 fiscal year a new pension plan for our Management Board was introduced. The plan is a defined contribution plan, with a pensionable age of 65 years. The employee contribution is set at 7% of the pensionable salary (base pay minus an offset). The table below outlines the annual contribution rates, including the employee contribution. The risk premium for the survivor's pension is financed separately by the employer.



## Corporate governance continued

Total contribution rates for our Management Board members are:

Age	Contribution rate
25 to 30	8.4%
30 to 35	10.2%
35 to 40	12.5%
40 to 45	15.2%
45 to 50	18.7%
50 to 55	23.0%
55 to 60	28.6%
60 to 65	36.1%

### Management Board

The total remuneration and related costs (excluding share-based payments – see information below on stock options and performance stock) of the members of the Management Board over the past two years, is as follows:

In thousands of Euro

Year ended December 31,	2009	2008 <sup>1</sup>
Salaries	<b>1,447</b>	1,259
Bonuses and one-off awards	<b>2,032</b>	782
Option costs	<b>1,212</b>	406
Pension costs	<b>316</b>	260
Other	<b>44</b>	39
	<b>5,051</b>	<b>2,746</b>

<sup>1</sup> Cees de Jong's remuneration for the year 2008 is included pro rata as of May 31, 2008.

The remuneration of the individual members of our Management Board during 2009, excluding stock options, was as follows:

Name	Salaries	Bonuses <sup>1</sup>	One-off awards	Option costs <sup>2</sup>	Pension costs <sup>3</sup>	Other costs <sup>4</sup>	Total
R.H.P. Brus	455	308	384	451	95	—	1,693
L. Kruimer	300	157	274	230	75	13	1,049
C. de Jong	331	173	274	289	49	12	1,128
J. Goudsmit	361	188	274	242	97	19	1,181
Totals	1,447	826	1,206	1,212	316	44	5,051

<sup>1</sup> Bonus expense includes the STI plan to which the Management Board is entitled as at December 31, 2009.

<sup>2</sup> The option costs are the costs recognized under IFRS and are not equal to the amounts involved in option exercises. In 2009, 250,000 options with an exercise price of € 9.4 and 20,000 options with an exercise price of € 3.49 were exercised by Ronald Brus with a total market value of € 1,801 and 85,000 options were exercised by Jaap Goudsmit with an exercise price of € 9.4 with a market value of € 538.

<sup>3</sup> 'Pension Costs' include pensions, social security costs and disability insurance.

<sup>4</sup> 'Other costs' include company cars.

Pension, retirement and similar arrangements for our Management Board members consist of the defined contribution plan, and we do not have further pension obligations beyond the annual premium contribution.

The Company's Management Board members held the following options for the period ended December 31, 2009:

Name of holder	Options held at December 31, 2008	Present status	Fair value per share at grant-date	Year of grant	Year of expiration	Exercise price	Granted 2009	Exercised 2009	Options held at December 31, 2009
R.H.P. Brus	250,000	Unconditional		2004	2009	9.40	—	(250,000)	—
	200,000	Unconditional		2003	2011	3.49	—	(20,000)	180,000
	90,000	Unconditional		2003	2011	2.64	—	—	90,000
	125,000	Unconditional		2003	2011	5.94	—	—	125,000
	300,000	Conditional	3.40	2008	2013	12.23	—	—	300,000 <sup>1</sup>
	—	Conditional	9.23	2009	2016	10.82	36,170	—	36,170 <sup>2</sup>
L. Kruimer	30,000	Unconditional		2003	2011	3.49	—	—	30,000
	125,000	Unconditional		2003	2011	5.94	—	—	125,000
	150,000	Conditional	3.40	2008	2013	12.23	—	—	150,000 <sup>1</sup>
	—	Conditional	9.23	2009	2016	10.82	19,490	—	19,490 <sup>2</sup>
C. de Jong	185,000	Conditional <sup>3</sup>	5.15	2007	2012	14.58	—	—	185,000
	200,000	Conditional	3.40	2008	2013	12.23	—	—	200,000 <sup>1</sup>
	—	Conditional	9.23	2009	2016	10.82	20,655	—	20,655 <sup>2</sup>
J. Goudsmit	85,000	Unconditional		2004	2009	9.40	—	(85,000)	—
	125,000	Unconditional		2003	2011	5.94	—	—	125,000
	150,000	Conditional	3.40	2008	2013	12.23	—	—	150,000 <sup>1</sup>
	—	Conditional	9.23	2009	2016	10.82	23,388	—	23,388 <sup>2</sup>
<b>Totals</b>	<b>2,015,000</b>						<b>99,703</b>	<b>(355,000)</b>	<b>1,759,703</b>

<sup>1</sup> At the annual General Meeting of Shareholders in 2008, the shareholders of the Company approved an additional option grant to the Management Board of 800,000 options. The options are conditionally granted and vest at the end of a three-year performance period starting June 2, 2008. The conditionally granted options include a market condition that is taken into account when estimating the fair value of the equity instruments granted. The market condition is an absolute total shareholder return of plus 50% share value measured three years after the grant.

<sup>2</sup> All options granted to the Management Board in 2009, are conditionally granted LTI options. At the annual General Meeting of Shareholders in 2008, the shareholders of the Company approved the revised LTI plan for the Management Board. Under the terms of the LTI plan, options are conditionally granted and vest at the end of a three-year performance period. The conditionally granted options include a market condition that is taken into account when estimating the fair value of the equity instruments granted. The number of LTI options that vest are based on the fulfillment of the LTI performance condition. On the vesting date, the Company's Total Shareholder Return ('TSR') performance is measured against the performance of the NASDAQ Biotechnology Index during the performance period. The positive difference in percentages, if any, between the Company's TSR compared to the performance of the NASDAQ Biotechnology Index, determines the number of LTI options that vest on the vesting date. Depending on the level of achievement of these market measures, at the end of three years, the number of shares vesting could be 0%-200% of the number of options originally granted.

<sup>3</sup> The option tranche granted to Cees de Jong on September 1, 2007 was not granted in his capacity as Board Member. The average fair value of the options was € 5.15. The vesting period of these options is four years and every year 25% of the options vest. The corresponding compensation costs of the options are recognized in accordance with the accelerated method. As at January 1, 2009 a number of 46,250 options were unconditional. The remaining 138,750 were still subject to non-market vesting conditions.

## Corporate governance continued

The Company's Management Board members held the following shares in the Company at December 31, 2009:

Name of holder	Ordinary shares held at December 31, 2009	% of total ordinary shares
R.H.P. Brus	239,202	0.29%
L. Kruimer	28,195	0.03%
C. de Jong	5,406	0.01%
J. Goudsmit	169,276	0.21%
	442,079	0.54%

The following table describes loans granted to the Group's Management Board and senior management since January 1, 2001. The Company has not granted any loans to any Supervisory Board members. The Company sets interest rates on these loans in relation to Dutch income tax law. The loans were granted to the persons listed below in connection with options granted to them on the Company's ordinary shares. These loans become payable at the time shares received on exercise of the related options are sold or immediately in case the employee ceases to work for the Company before this time. The Company funded the loans prior to July 30, 2002, the date legislation was passed in the US prohibiting the granting of additional loans to company officers.

Name	outstanding since January 1, 2001	Largest amount of loan at December 31, 2009	Amount of loan outstanding at 2009 interest rate in %
R.H.P. Brus	132	87	3.5%
Other personnel	61	47	3.5%

The Group is not a party to any material transactions, or proposed transactions, in which any director, any executive officer, any spouse or relative of any of the foregoing, or any relative of any such spouse had, or was to have, a direct or indirect material interest other than those transactions disclosed in these financial statements.

### Supervisory Board

Due to the fact that the Group operates on a global scale with many of its supervisory directors used to the international arena, Crucell offers compensation to its supervisory directors in accordance with customary practice in the biotechnology sector.

Compensation for all Supervisory Board members consists of a fixed fee in cash and an annual share grant. The fixed fee in cash ranges from € 34 to € 44 per Supervisory Board member. In addition, the chairman of the Supervisory Board is awarded annually a net allowance of € 5 that is grossed up for taxation purposes. The annual share grant awarded to each member of the Supervisory Board equals 2,500 ordinary shares. The amounts will be revised on a triennial basis. The shares should be held for as long as an individual is a member of the Supervisory Board.

During 2009 and 2008, the individual members of the Supervisory Board were entitled to receive the following remuneration:

Name	Year ended December 31, 2009		Year ended December 31, 2008	
	Shares <sup>4</sup>	Cash fee	Shares <sup>4</sup>	Cash fee
J.P. Oosterveld <sup>1</sup>	2,500	54.2	2,500	54.2
A. Hoevenaars	2,500	35.0	2,500	35.0
S. Lance	2,500	34.0	2,500	34.0
Ph. Satow	2,500	35.0	2,500	35.0
C. Wilhelmsson	2,500	35.0	2,500	35.0
S. Davis	2,500	34.0	2,500	34.0
F. Waller <sup>2</sup>	2,500	34.0	—	—
D.S. Koechlin <sup>3</sup>	—	—	1,250	12.5
	<b>17,500</b>	<b>261.2</b>	<b>16,250</b>	<b>239.7</b>

<sup>1</sup> Mr. J.P. Oosterveld was appointed Chairman on June 2, 2006.

<sup>2</sup> Mr. F. Waller was appointed member of the Supervisory Board on June 5, 2009, but has attended meetings since January 2009.

<sup>3</sup> Mr. D.S. Koechlin resigned from the Supervisory Board on May 30, 2008.

<sup>4</sup> Instead of the share grant, a Supervisory Board member may also choose to receive a cash amount equaling the value of 2,500 shares at the date of grant minus 25%. No Supervisory Board member chose this option.

The Company's Supervisory Board members held the following options for the period ended December 31, 2009:

Name of Holder	Options held per December 31, 2008	Year of expiration	Exercise price €	Granted 2009	Exercised 2009	Forfeited 2009	Options held per December 31, 2009
J.P. Oosterveld	10,000	2009	8.81	—	10,000	—	—
	10,000	2009	11.55	—	10,000	—	—
S.P. Lance	10,000	2011	7.86	—	—	—	10,000
	10,000	2009	11.55	—	—	10,000	—
P.M. Satow	10,000	2009	11.55	—	10,000	—	—
	22,000	2011	3.49	—	—	—	22,000
	10,000	2011	6.48	—	—	—	10,000
C.E. Wilhelmsson	10,000	2009	11.55	—	10,000	—	—
	10,000	2011	6.48	—	—	—	10,000
A.Hoevenaars	5,000	2009	8.81	—	5,000	—	—
	10,000	2009	11.55	—	10,000	—	—
<b>Totals</b>	<b>117,000</b>			<b>—</b>	<b>55,000</b>	<b>10,000</b>	<b>52,000</b>

Crucell's Supervisory Board members held the following shares in the Company per December 31, 2009:

Name of holder	Ordinary shares held per December 31, 2009	% of total ordinary shares
J.P. Oosterveld	12,000	0.01%
A. Hoevenaars	10,000	0.01%
S.P. Lance	12,500	0.02%
P.M. Satow	75,210	0.09%
C.E. Wilhelmsson	10,000	0.01%
S. Davis	5,000	0.01%
F. Waller	—	0.00%
	<b>124,710</b>	<b>0.15%</b>

## Corporate governance continued

Pursuant to Dutch law, each member of Crucell's Supervisory Board and Management Board is responsible to the Company for the proper performance of his or her assigned duties. They are also responsible for taking measures to prevent the consequences of any improper performance of duties by another member of the Company's Supervisory Board or Management Board. The Company's articles of association provide that Crucell's Management Board members and Supervisory Board members are discharged from liability for their actions as board members, if the Company's General Meeting of Shareholders adopts a resolution to that effect.

This discharge extends only to actions or omissions disclosed in or apparent from the adopted annual accounts or otherwise communicated to the Company's General Meeting of Shareholders.

Mandatory provisions of Dutch law may limit this discharge of liability, for example in the case of bankruptcy. Under Dutch law, the Company's Supervisory Board members and members of the Company's Management Board generally cannot be held personally liable for decisions made exercising their reasonable business judgment.

The Company's articles of association provide that the Company shall generally indemnify any person who is or was a member of the Company's Supervisory Board or of the Management Board or one of the Company's employees, officers or agents, and suffers any loss as a result of any action in connection with their service to the Company, provided they acted in good faith in carrying out their duties.

This indemnification generally will not be available if the person seeking indemnification acted with gross negligence or willful misconduct in the performance of his or her duties to the Company. A court in which an action is brought, may however determine that indemnification is appropriate nonetheless.

### Shareholdings of the Management and Supervisory Board at most practicable date

As of March 29, 2010 members of our Management Board and Supervisory Board held the following ordinary shares and options.

Name of Holder	Ordinary shares held per March 29, 2010	Options held per March 29, 2010	Year of expiration	Exercise price (€)
R.H.P. Brus	239,202	140,000	2011	3.49
		90,000	2011	2.64
		125,000	2011	5.94
		300,000	2013	12.23
		36,170	2016	10.82
L. Kruimer	28,195	29,358	2017	13.96
		10,000	2011	3.49
		75,000	2011	5.94
		150,000	2013	12.23
		19,490	2016	10.82
C. de Jong	5,406	15,550	2017	13.96
		185,000	2012	14.58
		200,000	2013	12.23
		20,655	2016	10.82
		17,102	2017	13.96
J. Goudsmit	169,276	150,000	2015	14.01
		125,000	2011	5.94
		150,000	2013	12.23
		23,388	2016	10.82
<b>Totals</b>	<b>442,079</b>	<b>1,880,373</b>		
J.P. Oosterveld	14,500	—	—	—
A. Hoevenaars	12,500	—	—	—
S.P. Lance	15,000	10,000	2011	7.86
P.M. Satow	77,710	22,000	2011	3.49
		10,000	2011	6.48
C.E. Wilhelmsson	12,500	10,000	2011	6.48
S. Davis	7,500	—	—	—
F. Waller	2,500	—	—	—
<b>Totals</b>	<b>142,210</b>	<b>52,000</b>		

## Principal accountant fees and services

Deloitte Accountants B.V. audited the accompanying consolidated statements of financial position of Crucell N.V. and subsidiaries (the 'Group') as of December 31, 2009 and 2008 and the related consolidated statements of income, comprehensive income, changes in equity, and cash flows for each of the 3 years in the period ended December 31, 2009.

The Sarbanes-Oxley Act of 2002 requires that Audit Committees pre-approve all services provided by the Company's external auditor. This process is critical to the auditor maintaining independence. Our process requires that all services provided by the external auditor are pre-approved by the Audit Committee.

During 2009 and 2008, we paid the following amounts to our external auditors for audit services, audit related services and tax services.

Year ended December 31,	2009	2008
Audit fees	825	840
Audit related fees	149	75
Fees for services related to Consultations on tax matters	—	—
<b>Total</b>	<b>974</b>	<b>915</b>

Audit fees include fees associated with the annual audit, interim reviews, required statutory audits and services that only the external auditor can reasonably provide, such as services associated with documents issued in connection with securities offerings.

Audit-related fees include accounting consultations on financial and accounting reporting standards.

## Responsibility statement

Crucell's Management Board, as required by section 5.25c paragraph 2c of the Dutch Act on Financial Supervision (Wet op het Financieel Toezicht), confirms that to the best of their knowledge:

- The financial statements of 2009 give a true and fair view of the assets, liabilities, financial position and the profit or loss of the Group;
- The Annual Report gives a true and fair view of the position as per December 31, 2009 and the developments during 2009 of the Group; and
- The Annual Report contains a description of the principal risks that the Group faces.

## Controls and procedures

### Internal risk management and control system

Crucell's Management Board is responsible for designing, implementing and operating the Company's internal risk management and control systems. The purpose of these systems is to manage in an effective and efficient manner the significant risks to which the Company is exposed. Crucell's internal and risk management and control systems with respect to financial reporting are in line with the guidance set forth in the COSO model, an integrated internal control framework established by the Committee of Sponsoring Organizations of the Treadway Commission. The Company's internal risk management and control systems are designed to provide reasonable assurance that strategic objectives can be met. Such systems can never provide absolute assurance regarding achievement of Company objectives, nor can they provide an absolute assurance that material errors, losses, fraud, and the violation of laws or regulations will not occur. A summary of the risks that could prevent Crucell from realizing its objectives is included in the section 'Risk Factors' of this report.

Our internal risk management and control systems make use of various measures including:

- Annual strategic evaluations of our business;
- Periodic operational review meetings of the Management Board with the Management Committee;
- Quarterly financial planning meetings of the Management Board with the Supervisory Board;
- A planning and control cycle consisting of annual, quarterly and monthly procedures, including subsequent follow-up on achievements of targets set;
- Advice of Crucell's Disclosure Committee to our Chief Executive Officer and Chief Financial Officer with respect to the timely review, disclosure and evaluation of periodical (financial) reports as well as with respect to the maintenance and evaluation of disclosure controls and procedures;
- Letters of representation that are signed by selected key-management members on a quarterly basis in which they confirm that for their area of responsibility based upon their knowledge:
  - An effective system of internal controls and procedures is maintained; and
  - The financial reports fairly present the financial position, results of operations and cash flows;



## Corporate governance continued

- Management letters and audit reports provided by our external auditor;
- Internal Audit function which monitors the effectiveness of our internal risk management and control system. The Internal Audit function performs risk based systematic and ad hoc audits. The main findings are reported to the CFO and Audit Committee. The Internal Auditor regularly meets with the external auditor to discuss planning and findings of the internal audits performed;
- Crucell's standardized and formalized working practices; including the Biological Safety Manual which was developed in-house to meet the specific needs of Crucell's working environment;
- A Global crisis management policy, which was established in 2009. Crisis management and in particular crisis communications are key topics to Crucell in light of its size, growth potential and varied business divisions. By means of having clear procedures and responsibilities we ensure that the proper actions are taken whenever possible and that the Company's reputation is protected by timely, clear and consistent messaging to internal and external audiences; and
- The Crucell Code of Conduct.

The Management Board has discussed the internal risk management and control system with the Audit Committee and the Supervisory Board.

As a result of its listing at NASDAQ, Crucell is also obliged to comply with Section 404 of the Sarbanes-Oxley Act of 2002 and related regulations (Section 404). Section 404 addresses the responsibility of the Management Board for establishing and maintaining an adequate system of internal control over financial reporting. Internal control over financial reporting is a process to provide reasonable assurance regarding the reliability of our public financial reporting.

### Evaluation of disclosure controls and procedures

We have evaluated, with the participation of our Chief Executive Officer and Chief Financial Officer, the effectiveness of our disclosure controls and procedures as of December 31, 2009. There are inherent limitations to the effectiveness of any system of disclosure controls and procedures, including the possibility of human error and the circumvention or overriding of the controls and procedures. Accordingly, even effective disclosure controls and procedures can only provide reasonable assurance of achieving their control objectives. Based upon our evaluation, our Chief Executive Officer and Chief Financial Officer concluded that the disclosure controls and procedures as of December 31, 2009 were effective to provide reasonable assurance that information required to be disclosed in the reports we file or submit under the US Securities Exchange Act of 1934, as amended, is recorded, processed, summarized and reported, within the time periods specified in the applicable rules and forms, and that it is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate to allow timely decisions regarding required disclosure.

### Management's Report on Internal Control over Financial Reporting

Management of the Company is responsible for establishing and maintaining adequate internal control over financial reporting as defined in Rules 13a-15(f) and 15d-15(f) under the US Securities Exchange Act of 1934. The Company's internal control over financial reporting is designed to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. The Company's internal control over financial reporting includes those policies and procedures that:

- Pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions and disposition of the assets of the Company;
- Provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the Company are being made only by authorized employees in accordance with documented authorizations; and
- Provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use or disposition of the Company's assets that could have a material effect on the financial statements.

Because of its inherent limitations, internal control over financial reporting may not prevent or detect misstatements. Also, projections of any evaluation of effectiveness for future periods are subject to the risk that controls may become inadequate because of changes in conditions, or that the degree of compliance with policies or procedures may deteriorate.

As required by Section 404 of the Sarbanes-Oxley Act of 2002, Management assessed the effectiveness of the Company's internal control over financial reporting as of December 31, 2009. In making this assessment, Management used the criteria set forth by the Committee of Sponsoring Organizations of the Treadway Commission (COSO) in Internal Control-Integrated Framework.

Based on its assessment and those criteria, Management concluded that the Company maintained effective internal control over financial reporting as of December 31, 2009.

Deloitte Accountants B.V., the independent registered public accounting firm that audited the financial statements included in this Annual Report, has issued an attestation report on the effectiveness of the Company's internal control over financial reporting as of December 31, 2009 as stated in their report beginning on page 154 of this report.

#### **Changes in internal control over financial reporting**

There has not been any change in the internal controls over financial reporting of the Company that occurred during the period covered by this report that has materially affected, or is reasonably likely to materially affect, such internal controls over financial reporting.

# Report of independent registered public accounting firm

## To the Supervisory Board and Shareholders of Crucell N.V. Leiden, the Netherlands

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We have audited the internal control over financial reporting of Crucell N.V. and subsidiaries (the 'Company') as of December 31, 2009, based on criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission. The Company's management is responsible for maintaining effective internal control over financial reporting and for its assessment of the effectiveness of internal control over financial reporting, included in the accompanying Management's Report on Internal Control over Financial Reporting. Our responsibility is to express an opinion on the Company's internal control over financial reporting based on our audit.

We conducted our audit in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether effective internal control over financial reporting was maintained in all material respects. Our audit included obtaining an understanding of internal control over financial reporting, assessing the risk that a material weakness exists, and testing and evaluating the design and operating effectiveness of internal control based on the assessed risk, and performing such other procedures as we considered necessary in the circumstances. We believe that our audit provides a reasonable basis for our opinion.

A Company's internal control over financial reporting is a process designed by, or under the supervision of, the Company's principal executive and principal financial officers, or persons performing similar functions, and effected by the company's board of directors, management, and other personnel to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. A company's internal control over financial reporting includes those policies and procedures that (1) pertain to the maintenance of records that, in reasonable detail, accurately and fairly reflect the transactions

and dispositions of the assets of the company; (2) provide reasonable assurance that transactions are recorded as necessary to permit preparation of financial statements in accordance with generally accepted accounting principles, and that receipts and expenditures of the company are being made only in accordance with authorizations of management and Directors of the Company; and (3) provide reasonable assurance regarding prevention or timely detection of unauthorized acquisition, use, or disposition of the company's assets that could have a material effect on the financial statements.

Because of the inherent limitations of internal control over financial reporting, including the possibility of collusion or improper management override of controls, material misstatements due to error or fraud may not be prevented or detected on a timely basis. Also, projections of any evaluation of the effectiveness of the internal control over financial reporting to future periods are subject to the risk that the controls may become inadequate because of changes in conditions, or that the degree of compliance with the policies or procedures may deteriorate.

In our opinion, the Company maintained, in all material respects, effective internal control over financial reporting as of December 31, 2009, based on the criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the consolidated financial statements as of and for the year ended December 31, 2009 of the Company and our report dated April 6, 2010 expressed an unqualified opinion on those financial statements and included an explanatory paragraph regarding the change in the accounting policy adopted by the Company.

### **Deloitte Accountants B.V.**

Amsterdam, The Netherlands  
April 6, 2010

# Articles of association and share capital

## Memorandum and Articles of Association

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Set out below is a summary of material information concerning our shares, which are our ordinary shares together with our preference shares, and related material provisions of our articles of association and of Book 2 of the Dutch Civil Code (Boek 2 van het Burgerlijk Wetboek). This summary is not complete and is qualified in its entirety by reference to our articles of association and to Dutch law.

### General

We were incorporated as a limited liability company (naamloze vennootschap) on October 9, 2000 by deed executed before Mr. R.J.J. Lijdsman, civil law notary. Our corporate seat is in Leiden, the Netherlands, and we have offices at Archimedesweg 4-6, 2333 CN Leiden, the Netherlands. We are registered in the trade register of the Chamber of Commerce and Industry for Leiden under number 28087740. The statement of no objection of the Minister of Justice in respect of our deed of incorporation was issued on October 9, 2000 under number N.V. 1133178. Our agent in the US is CT Corporation, 111 Eighth Avenue, New York, New York 10011. Our articles of association were last amended on June 12, 2009 before Mr. R.J.J. Lijdsman, civil law notary.

### Corporate purpose

The objects of the Company are set out in Article 3 of the articles of association. Our objects include acquiring, establishing and managing companies in our field, controlling and using intellectual property, and funding of our operations as well as to do all that is connected therewith or may be conducive thereto.

### Limitation of liability and indemnification matters

Pursuant to Dutch law, each member of our Supervisory and Management Boards is responsible to us for the proper performance of his or her assigned duties. They are also responsible for taking measures to prevent the consequences of any improper performance of duties by another member of our Supervisory Board or our Management Board. Our articles of association provide

that our Management Board members and our Supervisory Board members are released from liability for the exercise of their duties as board members, if our General Meeting of Shareholders adopts a resolution to that effect. This discharge extends only to the exercise of the duties reflected in the annual accounts or otherwise disclosed to our General Meeting of Shareholders prior to the adoption of the annual accounts.

This release of liability may be limited by virtue of Dutch law, such as in the case of bankruptcy. Under Dutch law, our Supervisory Board members and members of our Management Board generally cannot be held personally liable for actions taken in their capacity as such, provided, however, that the foregoing shall not eliminate or limit the liability (1) for any breach of such individual's duty of loyalty to the Company or its shareholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) for any transaction from which the member derived an improper personal benefit or (4) for personal liability which is imposed by Dutch law, as may be amended from time to time.

Our articles of association provide that we shall generally indemnify any person who is or was a member of our Supervisory Board or our Management Board, and suffers any loss as a result of any action in connection with the execution of his duties for us, provided he acted in good faith and in a manner he reasonably believed to be in or not opposed to our best interests, and with respect to criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful or beyond his mandate.

This indemnification generally will not be available if the person seeking indemnification was adjudged liable for acting with gross negligence or willful misconduct in the performance of his duties to us, unless the court in which the action was brought, determines that indemnification is appropriate nonetheless.

## Articles of association and share capital continued

### Share capital

Our authorized share capital amounts to € 75,000,000 divided into: 156,250,000 ordinary shares and 156,250,000 preference shares, each with a par value of € 0.24.

At December 31, 2009, there were 81,446,295 ordinary shares issued and outstanding. No preference shares are currently issued and outstanding. The ordinary shares can be issued in bearer or registered form. The preference shares can only be issued in registered form. Only bearer ordinary shares can trade on NYSE Euronext Amsterdam. No share certificates will be issued for shares in registered form.

### Ordinary shares

Our ordinary shares may be in registered or bearer form and will be in bearer form unless the shareholder indicates otherwise in writing.

### Bearer ordinary shares

All of our bearer ordinary shares are embodied in a single global share certificate which will not be exchanged for single or multiple physical securities and which we will deposit with the Dutch Securities Depository (NECIGEF) for safekeeping on behalf of the parties entitled to the ordinary shares in bearer form.

The ordinary shares represented by the single global share certificate may only be transferred through the book-entry system maintained by NECIGEF. A participant in the collective deposit (verzameldepot) of a securities institution admitted to NECIGEF may, at his own expense, require conversion of one or more of his bearer ordinary shares into ordinary shares in registered form.

### Registered ordinary shares

We enter holders of registered ordinary shares in the register of shareholders. We do not issue share certificates. However, the shareholder may request an extract from the shareholders' register regarding the ordinary shares registered in his name. We are required to provide this free of charge. Dutch law requires that transfers of registered ordinary shares be

recorded in a written instrument to which we are a party or which is served on us, or that the transaction is acknowledged by us.

### Preference shares

As of the date of this Annual Report, we have not issued any preference shares. On October 25, 2000, we established a foundation called Stichting Preferente Aandelen Crucell, also referred to as the Preferred Foundation. The Preferred Foundation's objective is to safeguard our interests, our business and parties connected therewith by blocking any influences that may threaten these interests, which interests may include the continuity of the Company, identity of the proposed acquirer or identity of us, our business and the parties connected therewith. The Preferred Foundation can safeguard these interests through acquiring and managing our preference shares and by exercising the rights attaching to these shares, in particular, the voting rights.

The Preferred Foundation has an option to acquire preference shares up to 100% of the number of our outstanding shares, necessary to match the total number of statutory votes on all of the ordinary shares outstanding at the time of an acquisition. The Preferred Foundation must pay at least 25% of the nominal value of the preference shares it acquires from us. If we acquire any preference shares, they may be cancelled.

A board of governors of up to five persons directs the Preferred Foundation. Jan Oosterveld, in his capacity as chairman of our Supervisory Board, and Pieter Bouw, Mick W. den Boogert, Sweder van Wijnbergen and Gerard P. Krans, have been appointed to the board of governors. A majority of these members may not be members or former members of our Management or Supervisory Board, or an employee of any of our advisers, any of our banks or us. These independent members are appointed by the board of governors. The non-independent members are appointed by our Supervisory Board after consultation with our Management Board.

Membership of the board of governors of the Preferred Foundation terminates upon:

- Voluntary retirement, reaching the age of 72, death or bankruptcy;
- For our non independent members, resignation, or dismissal by the members of our Supervisory Board;
- For our independent members, if they cease to be independent;
- Dismissal by the complete board of the Preferred Foundation; or
- Periodic retirement in accordance with a rotation plan to be drawn up by the Preferred Foundation's board of governors, however, these members may be reappointed.

### **Issue of shares and pre-emptive rights**

Our General Meeting of Shareholders, or our Management Board if the General Meeting of Shareholders has delegated the power to it, has the authority to decide on any further issuance of shares or rights to subscribe for shares and on the terms and conditions of such issuance. Our Management Board is the authorized corporate body (orgaan) for this purpose until November 30, 2010, and the authorization may at any time be extended by the General Meeting of Shareholders for periods of up to five years. Our Management Board's authority to issue shares is limited to a maximum of 10% of the issued share capital at the time of issue, plus a further issue up to 10% of the issued share capital at the time of issue in case the issue takes place in relation to a merger or an acquisition.

Our Management Board can issue shares of any class if it has the approval of our Supervisory Board. Without specific authorization from our General Meeting of Shareholders our Management Board may not issue preference shares or grant options for such shares if, as a result, more preference shares than ordinary shares will or could become outstanding.

Each holder of ordinary shares has pre-emptive rights to subscribe for any ordinary shares that we issue and has pre-emptive rights to subscribe if we grant rights to subscribe for ordinary shares. Pre-emptive rights are in proportion to the percentage of our outstanding ordinary shares that the holder owns. Pre-emptive rights do not apply to ordinary shares issued for a non-cash contribution, to ordinary shares issued to our employees or ordinary shares issued to a person who exercises a previously acquired right to subscribe for ordinary shares. Holders of preference shares do not have pre-emptive rights if we issue ordinary shares,

and holders of ordinary shares have no pre-emptive rights to purchase preference shares if we issue preference shares.

If our Management Board has been delegated the authority to issue shares, it can limit or exclude any pre-emptive rights as long as the general meeting of shareholders has granted it that power and our Supervisory Board approves. At present, our Management Board is authorized to do this. This authorization is valid until November 30, 2010 and the General Meeting of Shareholders may at any time extend this authorization for periods of up to five years.

Our shares cannot be issued below par. The ordinary shares must be fully paid up upon issue. Preference shares may be issued without being fully paid up, but at least one-quarter of the nominal amount must be paid up upon subscription, and each issue of preference shares must have the same amount paid up. Our Management Board may determine the day and the amount of a further call for payment on preference shares.

### **Acquisition by us of shares in our own capital**

We may acquire our own fully paid up shares if the following conditions are met:

- Our General Meeting of Shareholders has authorized our Management Board to acquire the shares;
- The authorization specifies the number of shares that we may acquire, the manner in which they may be acquired and the limits within which the price must be set;
- Our shareholders' equity, after deduction of the price of acquisition, is not less than the sum of the paid and called up portion of the share capital and the reserves that provisions of Dutch law or our articles of association require us to maintain; and
- The aggregate par value of the shares to be acquired, together with the shares in our share capital that we already hold directly, indirectly or as pledgee, does not equal more than one-tenth the aggregate par value of our total issued share capital.

An authorization by the General Meeting of Shareholders for a term of a maximum of 18 months is needed in the event of an acquisition for valuable consideration. Currently an authorization is granted to the Management Board by the General Meeting of Shareholders to repurchase fully paid up ordinary shares up to 10% of our outstanding share capital until November 30, 2010. The repurchase price lies between the nominal value of the shares and an amount equal to



## Articles of association and share capital continued

110% of the highest price officially quoted on the NASDAQ National Market and the NYSE Euronext Amsterdam stock exchange on any of five (5) banking days preceding the date of the repurchase.

We and our subsidiaries may not vote shares that we or they hold. We may acquire shares to transfer them to our employees or the employees of our group companies under designated stock option plans without authorization.

### Capital reduction

If our Management Board proposes, our Supervisory Board approves and Dutch law permits, the General Meeting of Shareholders can reduce our issued share capital by cancellation of shares or reduction of the nominal value of shares.

### Other key provisions of our articles of association

#### Voting rights and shareholders' meetings

We must hold annual general meetings of shareholders within six months of the end of our financial year. The annual meeting is held, among other things, to adopt our annual accounts. We must hold extraordinary general meetings of shareholders whenever:

- Shareholders and holders of American depositary receipts for shares together representing at least one-tenth of our outstanding share capital request it in writing, listing the topics to be discussed; and
- Our Management Board or our Supervisory Board deems appropriate.

General meetings of shareholders may only be held in the municipalities of Leiden, Amsterdam, Haarlemmermeer (including Schiphol Airport and Schiphol-Rijk), Utrecht, Rotterdam and The Hague.

Each shareholder can attend general meetings in person or by proxy, address the meeting and vote. Each share, whether ordinary or preference, confers one vote on the shareholder. The Management Board must be notified in writing of a

registered shareholder's intention to attend the General Meeting of Shareholders. The holders of bearer ordinary shares can vote if a NECIGEF participant sends a written statement as to their shareholdings to our offices. Resolutions are passed by absolute majority of votes cast unless stated otherwise in Dutch law and our articles of association.

Shareholders representing alone, or in aggregate, at least one percent (1%) of our issued capital or – according to the Euronext Official Price List – at least a value of 50 million Euro, have the right to request the Management Board and the Supervisory Board to place items on the agenda of the General Meeting of Shareholders. These requests shall be honoured on the condition:

- That the shareholders have a reasonable interest in the items to be considered;
- That the placing on the agenda is not in conflict with the orderly course of the meeting and that there shall be no material interest against placing the item on the agenda; and
- That the request has been filed in writing with the Management Board or the Chairman of the Supervisory Board at least 60 days prior to the date of the General Meeting of Shareholders.

The General Meeting of Shareholders can amend our articles of association, dissolve us, merge us or demerge us only if proposed by the Supervisory Board.

Dutch law and our articles of association do not impose any limitations on non-Dutch ownership or voting of our ordinary shares.

### Approval rights of the Supervisory Board

Our Supervisory Board must approve certain resolutions of our Management Board, which are specified in our articles of association.

## Annual Report

We have a calendar financial year. Dutch law requires that within four months after the end of our financial year, unless the general meeting of shareholders has extended this period for a maximum of six months, our Management Board must make available to the shareholders a report with respect to that financial year. This report must include the financial statements and a report of an independent accountant. The Annual Report is submitted to the annual General Meeting of Shareholders for adoption. See 'Information for Shareholders and Investors – Limitation of Liability and Indemnification Matters'.

## Dividends

Annual dividends may only be paid out of profits as shown in the adopted annual financial statements. We may not make distributions if the distribution would reduce our shareholders' equity below certain reserves required by Dutch law or by our articles of association. The profits must first be used to set up and maintain reserves required by Dutch law and must then be set off against certain financial losses. The dividends for the preference shares will be a certain percentage of their nominal value. These will be paid first. With Supervisory Board approval, our Management Board then decides whether and how much of the remaining profit they will reserve. Any profits remaining shall be paid as a dividend on the ordinary shares, if the retained earnings are negative or are to be used to form a statutory reserve no dividend will be paid out. With the approval of our Supervisory Board and subject to Dutch law, our Management Board can pay an interim dividend.

We can make distributions to shareholders at the charge of one or more of our reserves. Holders of shares are entitled to the full dividend for the financial year 2000 and subsequent financial years. Any dividends that are not claimed within five years of their declaration revert to us.

## Amendment of our articles of association and liquidation rights

The General Meeting of Shareholders may only resolve to amend our articles of association or to dissolve, merge or demerge us on the proposal of our Supervisory Board. The class of shareholders affected must approve a resolution to amend the articles of association to change the rights of the class. If we are dissolved and liquidated, after we pay all debts and liquidation expenses, the holders of preference shares have first rights to payment of any dividends not fully paid to them in previous years and of the nominal value of

their preference shares. Any remaining assets will be distributed to the holders of ordinary shares.

## Enforcement of civil liabilities

We are incorporated under the laws of the Netherlands, and the majority of the members of our Supervisory Board, all of the members of our Management Board and management team and all of the experts named in this document are residents of, and most of our and their assets are located in, jurisdictions outside the US. As a result, it may not be possible for you to effect service of process within the US upon us or these persons, or to enforce against us or these persons in courts in the US, judgments of these courts predicated upon the civil liability provisions of US securities laws. In addition, it is not clear whether a Dutch court would impose civil liability on us, members of our Management Board or Supervisory Board or management team or any of the experts named in this document in an original action based solely upon the federal securities laws of the US brought in a court of competent jurisdiction in the Netherlands. Dutch law, furthermore, does not recognize a shareholder's right to bring a derivative action on behalf of a corporation.

Our legal counsel in the Netherlands, Allen & Overy, has advised us that because there is no treaty on the reciprocal recognition and enforcement of judgments in civil and commercial matters between the US and the Netherlands, courts in the Netherlands will not automatically enforce a final judgment rendered by a US court. In order to obtain a judgment enforceable in the Netherlands, claimants must litigate the relevant claim again before a Dutch court of competent jurisdiction. Under current practice, however, a Dutch court will recognize a final and conclusive judgment rendered by a US court if the Dutch court finds that:

- The US court assumed jurisdiction on grounds that are acceptable from an international law perspective;
- The final judgment results from proceedings compatible with Dutch concepts of due process; and
- The final judgment does not contravene public policy of the Netherlands.

If the Dutch court recognizes the final US judgment, that court generally will grant the same judgment without the parties having to litigate again on the merits.

## Articles of association and share capital continued

### **Obligations of shareholders to disclose holdings under Dutch law**

Under the Financial Supervision Act any person who, directly or indirectly, acquires, or disposes of, an interest in the capital and/or the voting rights of a public limited liability company incorporated under Dutch law with an official listing on a stock exchange within the European Economic Area must immediately give written notice to the Dutch securities regulator AFM by means of a standard form, of such acquisition or disposal if, as a result of such acquisition or disposal, the percentage of capital interest and/or voting rights held by such person meets, exceeds or falls below the following thresholds: 5%, 10%, 15%, 20%, 25%, 30%, 40%, 50%, 60%, 75% and 95%.

The notification requirement also applies if a person's capital interest or voting right meets, exceeds or falls below the above mentioned thresholds as a result of a change in the share capital or voting rights, and the notification must be made no later than the fourth trading day after the AFM has published the notification as described in the following sentence. Crucell is required to notify the AFM immediately if its share capital or voting rights change by 1% or more since the previous notification. Other changes must be notified periodically.

In addition, the members of the Management Board and Supervisory Board are required to immediately notify the AFM of any change in the number of Crucell shares or options they hold or voting rights in respect of these shares. The AFM will disclose this information in a public register on its website. Non-compliance with the obligations of the Financial Supervision Act can lead to criminal prosecution. In addition, a civil court can issue orders against any person who fails to notify or incorrectly notifies in accordance with the Financial Supervision Act, including suspension of the voting rights in respect of such person's ordinary shares.

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# Report of independent registered public accounting firm

## To the Supervisory Board and Shareholders of Crucell N.V. Leiden, the Netherlands

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We have audited the accompanying consolidated statements of financial position of Crucell N.V. and subsidiaries (the 'Group') as of December 31, 2009, 2008 and January 1, 2007 and the related consolidated statements of income, consolidated statements of comprehensive income, consolidated statements of changes in equity, and consolidated statements of cash flows for each of the three years in the period ended December 31, 2009. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of the Group as of December 31, 2009 and 2008, and the results of their operations and their cash flows for each of the three years in the period ended December 31, 2009, in conformity with International Financial Reporting Standards as issued by the International Accounting Standards Board.

As discussed in note 1.5.1 to the financial statements as of January 1, 2009, the Group changed its method of accounting for defined benefit pension plans to recognize actuarial gains and losses directly in the period in which they occur in other comprehensive income, and retrospectively, adjusted the 2008 and 2007 financial statements for the change.

We have also audited, in accordance with the standards of the Public Company Accounting Oversight Board (United States), the Company's internal control over financial reporting as of December 31, 2009, based on the criteria established in Internal Control – Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission and our report dated April 6, 2010 expressed an unqualified opinion on the Company's internal control over financial reporting.

## Deloitte Accountants B.V.

Amsterdam, The Netherlands

April 6, 2010

# Consolidated statements of income

Year ended December 31,

(Amounts in thousands of Euro, except per share data)	Notes	2009	2008 As adjusted	2007 As adjusted
Product sales		304,439	226,055	177,569
License revenues		23,049	30,202	12,211
Service fees		10,675	10,900	14,006
<b>Total revenues</b>	4	<b>338,163</b>	<b>267,157</b>	<b>203,786</b>
Cost of product sales		(185,599)	(138,790)	(124,557)
Cost of service and license fees		(9,014)	(6,965)	(10,327)
<b>Total cost of sales</b>		<b>(194,613)</b>	<b>(145,755)</b>	<b>(134,884)</b>
<b>Gross margin</b>		<b>143,550</b>	<b>121,402</b>	<b>68,902</b>
Government grants		6,870	5,380	7,086
Other income		12,969	10,772	2,244
<b>Total other operating income</b>		<b>19,839</b>	<b>16,152</b>	<b>9,330</b>
Research and development		(70,176)	(70,229)	(63,995)
Selling, general and administrative		(61,400)	(64,778)	(63,566)
Reversal of impairment / (impairment)	5.6/5.7	7,199	4,888	(171)
<b>Total other operating expenses</b>		<b>(124,377)</b>	<b>(130,119)</b>	<b>(127,732)</b>
<b>Operating profit/(loss)</b>		<b>39,012</b>	<b>7,435</b>	<b>(49,500)</b>
Financial income	5.2	9,020	6,935	13,190
Financial expenses	5.3	(12,213)	(9,597)	(11,812)
Results investments non-consolidated companies	5.9	2,147	(128)	(996)
Results disposal of non-consolidated companies	5.9	—	1,570	2,186
Disposal of subsidiaries	1.1	—	(367)	—
<b>Profit/ (loss) before tax</b>		<b>37,966</b>	<b>5,848</b>	<b>(46,932)</b>
Income tax	5.4	(14,028)	8,402	2,598
<b>Profit/ (loss) for the year</b>		<b>23,938</b>	<b>14,250</b>	<b>(44,334)</b>
Attributable to:				
Equity holders of the parent		23,938	14,250	(44,334)
<b>Profit/ (loss) per share – basic</b>	5.5	<b>0.34</b>	<b>0.22</b>	<b>(0.68)</b>
<b>Profit/ (loss) per share – diluted</b>		<b>0.33</b>	<b>0.21</b>	<b>(0.68)</b>
Weighted average shares outstanding – basic (in thousands)		70,266	65,593	65,103
Weighted average shares outstanding – diluted (in thousands)		71,685	66,315	65,103

Following the accounting policy adoption to recognize actuarial gains and losses in other comprehensive income as of January 1, 2009, the entries for defined benefit post-employment plans were adjusted starting January 1, 2007. The impact of this retrospective application is provided in note 1.5.1. The accompanying notes are an integral part of these financial statements.



## Consolidated statements of comprehensive income

Year ended December 31,

(Amounts in thousands of Euro)

	Notes	2009	2008 As adjusted	2007 As adjusted
<b>Profit/(loss) for the period</b>		<b>23,938</b>	<b>14,250</b>	<b>(44,334)</b>
Foreign currency translation		13,266	(4,556)	(20,363)
Unrealized result on available for sale securities	3.5	5,219	(5,086)	(2,330)
Unrealized results on cash flow hedges	5.13	742	(685)	—
Actuarial gains and losses on pensions	5.10	(8,217)	(842)	1,804
Income tax	5.4	1,786	257	(388)
<b>Other comprehensive income for the period, net of tax</b>		<b>12,796</b>	<b>(10,912)</b>	<b>(21,277)</b>
<b>Total comprehensive income for the period</b>		<b>36,734</b>	<b>3,338</b>	<b>(65,611)</b>
Attributable to:				
Equity holders of the parent		36,734	3,338	(65,611)

Following the accounting policy adoption to recognize actuarial gains and losses in other comprehensive income as of January 1, 2009, the entries for defined benefit post-employment plans were adjusted starting January 1, 2007. The impact of this retrospective application is provided in note 1.5.1. The accompanying notes are an integral part of these financial statements.

# Consolidated statements of financial position

(Amounts in thousands of Euro)	Notes	December 31, 2009	December 31, 2008 As adjusted	January 1, 2007 As adjusted
<b>Assets</b>				
<b>Non-current assets</b>				
Property, plant and equipment	5.6	192,615	151,206	138,018
Intangible assets	5.7	75,398	79,004	113,077
Goodwill	5.8	46,824	46,076	47,419
Investments in associates and joint ventures	5.9	11,433	9,239	5,998
Pension asset	5.10	2,923	8,612	3,301
Available-for-sale investments	3.5	10,441	4,922	12,339
Deferred tax asset	5.4	208	—	308
Other financial assets	5.11	16,218	14,920	16,430
		<b>356,060</b>	<b>313,979</b>	<b>336,890</b>
<b>Current assets</b>				
Cash and cash equivalents	5.12	327,837	170,969	157,837
Derivative financial instruments	5.13	286	1,761	68
Trade accounts receivable	5.14	87,031	40,108	58,563
Inventories	5.15	118,420	91,847	75,519
Other current assets	5.16	121,497	17,633	25,084
		<b>655,071</b>	<b>322,318</b>	<b>317,071</b>
<b>Total assets</b>		<b>1,011,131</b>	<b>636,297</b>	<b>653,961</b>
<b>Liabilities and equity</b>				
Equity attributable to equity holders of the parent	5.17	738,265	452,534	497,683
<b>Non-current liabilities</b>				
Long-term provisions	5.19	6,853	5,876	5,380
Long-term financial liabilities	5.20	33,533	35,297	26,945
Deferred tax liabilities	5.4	18,830	16,644	33,701
Other non-current liabilities and deferred income	5.21	55,484	7,645	—
		<b>114,700</b>	<b>65,462</b>	<b>66,026</b>
<b>Current liabilities</b>				
Short-term provisions	5.19	739	1,581	2,874
Short-term financial liabilities	5.20	18,767	26,333	19,468
Other current liabilities and deferred income	5.21	47,512	28,405	29,132
Income tax payable		12,049	2,777	266
Trade accounts payable	5.22	79,099	59,205	38,512
		<b>158,166</b>	<b>118,301</b>	<b>90,252</b>
<b>Total liabilities</b>		<b>272,866</b>	<b>183,763</b>	<b>156,278</b>
<b>Total liabilities and equity</b>		<b>1,011,131</b>	<b>636,297</b>	<b>653,961</b>

Following the accounting policy adoption to recognize actuarial gains and losses in other comprehensive income as of January 1, 2009, the entries for defined benefit post-employment plans were adjusted starting January 1, 2007. The impact of this retrospective application is provided in note 1.5.1. The accompanying notes are an integral part of these financial statements.

## Consolidated statements of changes in equity

	Issued capital	Share premium	Net unrealized gains reserve	Hedging reserve	Actuarial gains / (losses) on pensions	Translation reserve	Accumulated deficit	Total equity
<b>At January 1, 2007</b>	<b>15,553</b>	<b>726,869</b>	<b>10,670</b>	—	—	<b>(7,933)</b>	<b>(247,273)</b>	<b>497,886</b>
Change in accounting policy	—	—	—	—	383	—	(586)	(203)
<b>At January 1, 2007 (As adjusted)</b>	<b>15,553</b>	<b>726,869</b>	<b>10,670</b>	<b>—</b>	<b>383</b>	<b>(7,933)</b>	<b>(247,859)</b>	<b>497,683</b>
Issue of shares	132	2,185	—	—	—	—	—	2,317
Cost of share-based payments	—	6,524	—	—	—	—	—	6,524
Total comprehensive income for the period	—	—	(2,330)	—	1,416	(20,363)	(44,334)	(65,611)
<b>At December 31, 2007 (As adjusted)</b>	<b>15,685</b>	<b>735,578</b>	<b>8,340</b>	<b>—</b>	<b>1,799</b>	<b>(28,296)</b>	<b>(292,193)</b>	<b>440,913</b>
Issue of shares	115	3,115	—	—	—	—	—	3,230
Cost of share-based payments	—	5,053	—	—	—	—	—	5,053
Total comprehensive income for the period	—	—	(5,086)	(685)	(585)	(4,556)	14,250	3,338
<b>At December 31, 2008 (As adjusted)</b>	<b>15,800</b>	<b>743,746</b>	<b>3,254</b>	<b>(685)</b>	<b>1,214</b>	<b>(32,852)</b>	<b>(277,943)</b>	<b>452,534</b>
Issue of shares	3,747	237,518	—	—	—	—	—	241,265
Cost of share-based payments	—	7,732	—	—	—	—	—	7,732
Total comprehensive income for the period	—	—	5,219	742	(6,431)	13,266	23,938	36,734
<b>At December 31, 2009</b>	<b>19,547</b>	<b>988,996</b>	<b>8,473</b>	<b>57</b>	<b>(5,217)</b>	<b>(19,586)</b>	<b>(254,005)</b>	<b>738,265</b>

Following the accounting policy adoption to recognize actuarial gains and losses in other comprehensive income as of January 1, 2009, the entries for defined benefit post-employment plans were adjusted starting January 1, 2007. The impact of this retrospective application is provided in note 1.5.1. The accompanying notes are an integral part of these financial statements.

# Consolidated statements of cash flows

Year ended December 31,

(Amounts in thousands of Euro)

Notes      2009      2008  
As adjusted      As adjusted

<b>Cash flows from (used in) operating activities</b>	5.27			
Profit/ (loss) before tax		<b>37,966</b>	5,848	(46,932)
Adjustments				
Results of investments in associates and joint ventures	5.9	<b>(2,147)</b>	128	996
Financial income and expenses	5.2/ 5.3	<b>(814)</b>	3,963	(1,378)
Amortization	5.7	<b>11,107</b>	11,674	11,894
Depreciation	5.6	<b>20,393</b>	16,629	14,453
(Reversal of impairment) / impairment	5.6/ 5.7	<b>(7,199)</b>	(4,888)	171
Change in pension assets	5.10	<b>5,658</b>	(750)	(3,871)
Non-cash change in long-term deferred income and provisions	5.19/5.20	<b>(15,722)</b>	(4,131)	13,276
Stock-based compensation	5.18	<b>7,732</b>	5,053	6,817
Other non-cash items		<b>85</b>	(139)	6,257
Changes in net working capital				
Trade accounts receivable and other current assets		<b>(44,527)</b>	4,191	7,968
Inventories		<b>(21,475)</b>	(37,121)	(6,128)
Trade accounts payable and other current liabilities		<b>38,253</b>	3,116	23,330
Interest paid		<b>(2,934)</b>	(2,684)	(2,152)
Income taxes paid		<b>(3,677)</b>	(576)	(1,545)
Receipts from / (payments of) deferred income and provisions		<b>54,167</b>	(567)	(962)
<b>Net cash flows from (used in) operating activities</b>		<b>76,866</b>	<b>(254)</b>	<b>22,194</b>
<b>Cash flows from (used in) investing activities</b>	5.28			
Purchase of property, plant and equipment	5.6	<b>(51,035)</b>	(15,787)	(27,156)
Proceeds from sale of equipment	5.6	<b>371</b>	—	113
Acquisition of intangible assets (including goodwill)	5.7/ 5.8	<b>(5,477)</b>	(237)	—
Acquisition of business	5.8	<b>(453)</b>	—	—
Proceeds from / (investments) non-consolidated companies	5.9	<b>—</b>	182	(2,472)
Proceeds from / (investments in) financial assets		<b>(100,047)</b>	2,540	—
Interest received	5.2	<b>2,254</b>	4,395	5,274
<b>Net cash flows (used in) investing activities</b>		<b>(154,387)</b>	<b>(8,907)</b>	<b>(24,241)</b>
<b>Cash flows from financing activities</b>	5.29			
Proceeds from issue of share capital	5.17	<b>241,265</b>	3,230	2,281
Proceeds from financial liabilities	5.20	<b>3,316</b>	35,732	10,309
Repayment of financial liabilities	5.20	<b>(13,069)</b>	(22,336)	(1,346)
<b>Net cash flows from financing activities</b>		<b>231,512</b>	<b>16,626</b>	<b>11,244</b>
<b>Total cash flow</b>		<b>153,991</b>	<b>7,465</b>	<b>9,197</b>
Effect of exchange rates on cash and cash equivalents		<b>2,877</b>	256	(3,786)
<b>Net increase in cash and cash equivalents</b>		<b>156,868</b>	<b>7,721</b>	<b>5,411</b>
Cash and cash equivalents at beginning of the year	5.12	<b>170,969</b>	163,248	157,837
<b>Cash and cash equivalents at end of the year</b>	5.12	<b>327,837</b>	<b>170,969</b>	<b>163,248</b>

Following the accounting policy adoption to recognize actuarial gains and losses in other comprehensive income as of January 1, 2009, the entries for defined benefit post-employment plans were adjusted starting January 1, 2007. The impact of this retrospective application is provided in note 1.5.1. The accompanying notes are an integral part of these financial statements.

# Notes to the consolidated financial statements

(Amounts in thousands of Euro, except per share data or as otherwise noted)

## 1 General information

### 1.1 Corporate information

#### General

Crucell N.V. (the 'Company') is incorporated and domiciled in Leiden, the Netherlands. Its shares are publicly traded on NYSE Euronext Amsterdam (CRXL), and SWX Swiss Exchange Zurich (CRX). Its American Depositary Shares (ADSs) are publicly traded on NASDAQ New York (CRXL). The Company and its subsidiaries together constitute the Crucell Group, or the 'Group'. The Company has subsidiaries in the Netherlands, Switzerland, Spain, Italy, Sweden, Korea, the United Kingdom and the US. The Group employed 1,248 people at December 31, 2009 (2008: 1,126).

Crucell is a fully integrated biopharmaceutical company, focused on developing, producing and marketing products to combat infectious diseases. Its core vaccine portfolio includes Inflexal V, a vaccine against influenza, paediatric vaccines Hepavax-Gene, Quinvaxem, Epaxal junior and MoRu-Viraten, and travel vaccines Vivotif, Dukoral, and Epaxal. In addition to these portfolio vaccines, the Group has a broad pipeline of new potential vaccines and proteins. The Group has developed various proprietary technologies such as PER.C6, MAbstrax, AdVac, STAR and virosome-adjuvanted technologies. The Group licenses these proprietary technologies to other companies in the biopharmaceutical industry.

#### Changes in the scope of consolidation

The consolidated financial statements include the results of the acquired companies for the period from the date of acquisition unless mentioned otherwise. There has been the following change in the scope of consolidation in 2009. On June 5, 2009 the Group established Crucell UK Ltd. On July 15, 2009 the Group purchased, via its subsidiary Crucell UK Ltd., selected assets and liabilities of UK-Based Masta Ltd. See note 5.8 'Goodwill and business combinations' for more information on this acquisition.

In 2008, the most significant change in the scope of consolidation was the sale of the Group's fully-owned subsidiary Etna Biotech Srl (Catania, Italy) to Zydus Cadila (Ahmadabad, India). The sale resulted in net proceeds for Crucell of € 182;

## List of consolidated companies

The Company's most significant subsidiaries as of December 31, 2009 were:

Name	Legal seat ownership	Country	2009 ownership	2008 ownership	2007 ownership
Crucell Holland B.V.	Leiden	Netherlands	100%	100%	100%
U-BiSys B.V.	Utrecht	Netherlands	100%	100%	100%
ChromaGenics B.V.	Amsterdam	Netherlands	100%	100%	100%
Crucell Switzerland AG (prior: Berna Biotech AG)	Bern	Switzerland	100%	100%	100%
Crucell Spain SA (prior: Berna Biotech España SA)	Madrid	Spain	100%	100%	100%
Crucell Italy Srl (prior: Berna Biotech Italia Srl)	Milano	Italy	100%	100%	100%
Etna Biotech Srl	Catania	Italy	—	—	100%
Berna Rhein B.V.	Leiden	Netherlands	100%	100%	100%
Crucell UK Ltd.	Shipley, Bradford	United Kingdom	100%	—	—
Berna Biotech Korea corp.	Seoul	Korea	100%	100%	100%
Crucell Holding Inc.	Wilmington, DE	United States	100%	100%	100%
Crucell Vaccines Inc.	Wilmington, DE	United States	100%	100%	100%
Crucell Biologics Inc.	Wilmington, DE	United States	100%	100%	100%
SBL Vaccin Holding AB	Stockholm	Sweden	—	—	100%
Crucell Sweden AB (prior: SBL Vaccin AB)	Stockholm	Sweden	100%	100%	100%
Vitec AB	Stockholm	Sweden	—	—	100%

## Joint venture and associated companies (not consolidated)

Name	Joint venture/associate ownership	Legal seat ownership	Country	2009 ownership	2008 ownership	2007 ownership
Percivia LLC	Joint venture	Cambridge, MA	United States	50.0%	50.0%	50.0%
ADImmune corp.	Associated company	Taipei	Republic of China	11.8%	11.8%	20.0%
Kenta Biotech AG*	Sold	Bern	Switzerland	—	—	22.0%

\* On July 3, 2008 the Group sold all of the 2,625,000 shares it owned in Kenta Biotech AG to Inagro Finanz AG. Prior to this sale, our ownership interest had already been diluted from 37% in 2006 to 22% by the end of 2007. We realized an accounting gain of € 1,570 on the sale.

## 1.2 Basis of preparation

The consolidated financial statements of the Group have been prepared in accordance with International Financial Reporting Standards (IFRS) as issued by the International Accounting Standards Board (IASB) and are prepared on a historical cost basis unless stated otherwise. There are no differences between IFRS applied by the Group and IFRS as endorsed by the EU.

As permitted by article 362 of Book 2 of the Netherlands Civil Code, the company financial statements have been prepared applying the same IFRS accounting policies as used in the consolidated financial statements. In conformity with article 402, Book 2 of the Dutch Civil Code, the Company statement of income is presented in abbreviated form.

The financial statements for the year ended December 31, 2009 were authorized for issue in accordance with a director's resolution on April 6, 2010.

## Foreign currency translation

The functional and presentation currency of the Company is the Euro. All values are rounded to the nearest thousand (€ 000) unless indicated otherwise.

Each entity in the group determines its own functional currency based on the primary economic environment in which the entity operates. Items included in the financial statements of each entity are measured using that functional currency. Transactions in foreign currencies are initially recorded in the functional currency rate ruling at the date of the transaction. Monetary assets and liabilities denominated in foreign currencies are retranslated at the functional currency rate of exchange ruling at the year-end. All differences are taken to the statement of income. Non-monetary items that are measured in terms of historical cost in a foreign currency are translated using the exchange rates as at the dates of the initial transactions. Non-monetary items measured at fair value in a foreign currency are translated using the exchange rates at the date when the fair value was determined.



# Notes to the consolidated financial statements continued

At the reporting date, the assets and liabilities of subsidiaries with different functional currencies are translated into Euro at the rate of exchange ruling at the year-end and their statements of income and statements of cash flows are translated into Euro at the weighted average exchange rates for the year. The exchange rate differences arising on the translation are taken directly to the translation reserve, a separate component of equity.

## 1.3 Basis of consolidation

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The consolidated financial statements comprise the financial statements of the Company and its subsidiaries per December 31 and for the period then ended. The financial statements of the subsidiaries are prepared for the same reporting year as the Group, using consistent accounting policies. All intra-group balances and transactions are eliminated in full.

### Subsidiaries

Subsidiaries are entities controlled by the Company. Control is achieved where the Company has the power to govern the financial and operational policies of an enterprise so as to obtain benefits from its activities. Subsidiaries are fully consolidated from the date of acquisition, which is the date on which the Group obtains control, and continue to be consolidated until the date such control ceases.

### Joint ventures

A joint venture is a contractual arrangement whereby two or more parties undertake an economic activity that is subject to joint control. A jointly controlled entity is a joint venture that involves the establishment of a separate entity in which each venturer has an interest. The Group recognizes its interest in joint ventures using the equity method. Under the equity method, the investment in the joint venture is carried in the statement of financial position at cost plus post-acquisition changes in the Group's share of net assets of the joint venture. The statement of income reflects the share of the results of operations of the joint venture. Periodically the Group determines whether it is necessary to recognize an impairment loss with respect to the Group's

net investment in the joint venture. The reporting dates of the joint ventures are the same as those of the Group and the accounting policies of the joint ventures conform to those used by the Group.

### Associates

The Group's investments in associates are accounted for under the equity method of accounting and are initially recognized at cost. An associate is an entity in which the Group has significant influence and which is neither a subsidiary nor a joint venture. The reporting dates of the associates are the same as those of the Group and the associates' accounting policies conform to those used by the Group.

## 1.4 Use of estimates and judgments

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The preparation of financial statements requires Management to make judgments, estimates and assumptions that affect the application of accounting policies and the reported amounts of assets, liabilities, income and expenses. Actual results may differ from these estimates.

Estimates and underlying assumptions are reviewed on an ongoing basis. Revisions to accounting estimates are recognized in the period in which the estimate is revised and in any future periods affected. In particular, information about significant areas of estimation uncertainty and use of critical judgments in applying accounting policies that have the most significant effect on the amount recognized in the financial statements are described below.

### Revenue recognition

Sales transactions concluded by the Group may be complex as the underlying sales agreements can contain multiple components whose accounting treatment may be affected by the other components. Reviewing these agreements requires due care and a degree of management's judgment. Revenue is not recognized before it is assessed that significant risks and rewards of ownership have been transferred and that the Group retains no continuing managerial involvement or effective control over the goods

sold. For some transactions this can result in cash receipts being initially recognized as deferred income and then released to income over subsequent periods on the basis of the performance of the conditions specified in the agreement. The Group is also subject to various licensing agreements that contain milestones, which may only be recognized if they are 'substantive'.

On September 28, 2009 the Group entered into a strategic collaboration with affiliates of Johnson and Johnson ("JNJ"), which included among others an equity purchase agreement and two collaboration agreements. Management determined that the strategic collaboration should be viewed as one overall agreement as the commercial effect of the full transaction cannot be understood without reference to the series of agreements as a whole. This affects primarily the accounting treatment of the premium paid by JNJ over the shares issued. Management determined that, for accounting purposes, the premium on the shares is not warranted by the share issuance itself as it considered the price of the NYSE Euronext listed shares of the Company at the date of issuance to be the best fair value indicator. Hence the full premium in an amount of € 68,455 was allocated to the development programs. The premium was classified as deferred income and will be amortized over the duration of the continuing performance obligations of the development programs.

### Valuation of deferred tax assets and liabilities

Determination of income taxes in jurisdictions in which the Group operates requires exercising judgment. This involves estimating the actual current tax exposure together with assessing the valuation of carry forward losses and temporary differences. The temporary differences mainly relate to intangible assets, property, plant and equipment, inventories and pension assets.

In assessing the valuation of the deferred tax assets and liabilities the following items are considered: the future taxable profit projections, historical results, tax planning strategies, changes (substantively) enacted in tax laws and the specific timing of the recovery of deferred tax positions. In the event that actual results differ from these estimates due to future changes in income tax law or after final review of tax returns by tax authorities, the Group may need to adjust the valuation of its deferred tax assets and liabilities, which could materially impact the financial position and results of operations. Management believes that the estimates are reasonable.

As at December 31, 2009, the Group had unrecognized tax carry forward losses of € 180,261 (2008: € 172,732, 2007: € 254,511) that are available, with certain restrictions in time, for offset against future taxable profits of the companies in which the losses arose. Management assesses periodically the likelihood that the carry forward losses will be recovered from future taxable profit. If Management determines that recovery of carry forward losses is probable, a deferred tax asset is recognized. In 2008, a deferred tax asset of € 8,585 was recognized for carry forward losses of Crucell Switzerland AG, which was previously unrecognized due to lack of evidence of future taxable income. In 2009 this deferred tax asset was reduced by € 3,762 due to taxable profits. At the end of 2009 the total deferred tax assets for carry forward losses amounted to € 5,488 (2008: € 9,060, 2007: € 678)). To the extent the likelihood of deferred tax assets changes, an expense or a gain within the tax charge in our statement of income for the relevant period will be included.

### Impairment reviews

An impairment test on goodwill, and other assets that are not amortized, is performed annually and when there is an indication that the related CGU may be impaired. Other assets are tested when there is an indication that the asset is impaired.

For the purpose of impairment testing, assets are allocated to a cash generating unit (CGU). A CGU's recoverable amount is the higher of the CGU's fair value less costs to sell and its value in use. The Group starts its impairment reviews by determining the CGU's recoverable amount based on the fair value less costs to sell of an asset. If the fair value less costs to sell does not exceed the carrying amount, the Group will also consider the value in use before an impairment is recognized. The best evidence of a CGU's fair value less costs to sell is a price in a binding sale agreement in an arm's length transaction, adjusted for incremental costs that would be directly attributable to the disposal of the CGU. However for most of the Group's CGUs there are typically no observable market prices as the CGUs have a level of specificity for which no active market exists. The fair values less costs to sell are based on discounted net present value calculations that use assumptions applicable in the current market. Where applicable, the forecasted cash flows for pre-clinical programs are adjusted for the risk of failure of the program. See note 5.8 'Goodwill and business combinations' for more information on key assumptions.

## Notes to the consolidated financial statements continued

In December, 2006, an impairment loss of € 19,568 was recognized for two buildings, including installed equipment. Both buildings are located in Switzerland. Crucell Switzerland AG performed contract manufacturing and conducted a candidate vaccine development program in those buildings. The development of the candidate vaccine and the contract manufacturing were phased out during 2007. Consequently, the full carrying value of € 19,568 for the two buildings was impaired.

In the first quarter of 2008, the Group entered into an exclusive agreement with Wyeth Pharmaceuticals. The Group developed and manufactured certain components of a vaccine for use by Wyeth in clinical studies. The contract manufacturing takes place in one of the two buildings that were impaired in 2006. The Group reassessed the recoverable amount of the building and reversed € 5,219 of the previously recognized impairment loss. The depreciable life of the assets to which we reversed impairments was 18 months. The depreciable life was equal to the life assigned to the Wyeth contract.

In the third quarter of 2009, the Group reversed an impairment of € 8,084 relating to the buildings in Bern, Switzerland as alternative usages for both buildings were found. The buildings are now being used as development production sites for Epaxal and tuberculosis vaccines. The buildings have been adapted to the specific needs of the development programs, which avoided major spending in the construction of new development facilities. The Group reassessed the recoverable amount of the asset and reversed € 8,084 of the previously recognized impairment loss. This reversal was the maximum amount that could be reversed as the reversal of an impairment loss cannot be increased above the asset's carrying amount had no impairment loss been recognized in prior periods.

In 2009, there were several smaller impairments in Switzerland, Sweden, the Netherlands and Korea for individual items of property, plant and equipment totaling to an amount of € 885.

### Valuation of defined benefit plans

The pension liability recognized in the statement of financial position is the present value of the defined benefit obligation at the end of the financial year, less the fair value of the plan assets after adding or subtracting unrecognized past-service costs. The defined benefit obligation is calculated separately for each plan by estimating the amount of future benefit that employees have earned in return for their service in the current and prior periods. That benefit is discounted to determine its present value.

The assumptions used in the actuarial calculation can have a significant impact on the outcome. See note 5.10 'Retirement benefit obligations' for more information on the Group's principal assumptions used in determining the employee benefit obligations for the defined benefit plans. Changes in these key assumptions can have a significant impact on the defined benefit obligations, funding requirements and periodic costs incurred. The Group consults at least annually with external actuaries regarding these assumptions.

### Share-based payments

#### Option plans

The Company operates share-based payment programs, whereby in consideration for equity instruments both employees and non-employees render services.

The cost of equity-settled share-based option programs are measured by reference to the fair value at the date on which they are granted. The Company accounts for its stock options under the fair value method. See note 5.18 'Share-based payment plans' for more information on the Group's weighted average assumptions that were used in determining the fair value of the stock options.

Expected volatilities are based on historical volatilities of the Company's stock measured over a period commensurate with the expected term of the grants. The expected term used is based on the anticipated exercise behavior. Dividend yields used are based on historical information as to dividends declared by the Company. Risk-free interest rates used are

equal to the implied yield available on zero-coupon government bonds with a remaining term equal to the expected term of the share-based instrument.

Some of our share-based option programs include specific market-based conditions that are estimated at the time of the grant. Estimates of market based conditions that have an effect on the fair values of any shares or options allocated in our share based payment plans are share price growth on the stock markets and our Total Shareholder Return ('TSR') compared to an index of biotech companies. TSR reflects the return received by a shareholder, taking into account both the change in share price and dividends received, while assuming dividends are re-invested in the Company.

### **Recognition of provisions for litigations and claims**

Provisions are recognized when the Group has a present obligation (legal or constructive) as a result of a past event, it is probable that an outflow of resources embodying economic benefits will be required to settle the obligation and a reliable estimate can be made of the amount of the obligation. Management uses judgment in determining the provision for litigations and exposure to contingent liabilities related to pending litigation or other outstanding claims. Judgment is used in assessing the likelihood that a pending claim will succeed or a liability will arise and in quantifying the possible range of the final settlement.

The Group is subjected to (potential) lawsuits and other legal proceedings, resulting from the ordinary course of business. The current status of pending proceedings has been reviewed with legal counsel. Upon consideration of known relevant facts and circumstances, provisions were recognized for losses that are considered to be more likely than not and that can reasonably be estimated at the year-end.

## **1.5 Changes in accounting policies**

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### **1.5.1 New adopted accounting policies in the financial year 2009**

#### **Change in accounting policy**

In 2009, the Group changed its policy in accounting for actuarial gains and losses of defined benefit pensions plans. Starting 2009, the Group recognizes actuarial gains and losses in the period in which they occur in other comprehensive income. Previously the Group accounted for its actuarial gains and losses arising from experience-based adjustments and

changes in actuarial assumptions in line with the 'corridor' method as described in IAS 19.92.

Recognition of actuarial gains and losses when they occur provides more relevant and timely information, because it requires an employer to recognize all transactions and events of a defined benefit postretirement plan in comprehensive income in the period in which they occur. The Group believes that this view is confirmed by recent developments in the IASB and current accounting regulations as issued by the FASB, which propose to eliminate the smoothing and deferral mechanism of the "corridor" method.

In addition, the amount recognized in the statement of financial position can be reconciled more easily to the funded status of the defined benefit pension funds. The Group's only remaining difference between the funded status and the amount in the statement of financial position is the limitation on the recognized defined benefit assets recognized due to the 'asset ceiling'.

## Notes to the consolidated financial statements continued

The Group adjusted comparative amounts disclosed for each prior period presented as if the new accounting policy had always been applied. The impact on the December 31, 2009, 2008 and 2007 financial statements are as follows:

In thousands of Euro Year ended December 31,	2009			2008			2007		
	Before change	Impact	After Change	Before change	Impact	After Change	Before change	Impact	After Change
<b>Statement of income</b>									
Gross margin	143,550	—	143,550	121,402	—	121,402	68,902	—	68,902
Operating expenses	(132,084)	7,707	(124,377)	(129,691)	(428)	(130,119)	(125,918)	(1,814)	(127,732)
Profit (loss) before tax	30,259	7,707	37,966	6,276	(428)	5,848	(45,118)	(1,814)	(46,932)
Income Tax	(12,367)	(1,661)	(14,028)	8,310	92	8,402	2,208	390	2,598
Profit/(loss) for the year	17,892	6,046	23,938	14,586	(336)	14,250	(42,910)	(1,424)	(44,334)
<b>Statement of comprehensive income</b>									
Recognized income and (expense)	37,202	(468)	36,734	4,106	(768)	3,338	(65,624)	13	(65,611)
<b>Statement of financial position</b>									
As of December 31,									
<b>Statement of financial position</b>									
Provisions	5,671	1,921	7,592	6,158	1,299	7,457	5,334	233	5,567
Deferred tax liabilities	19,325	(495)	18,830	16,985	(341)	16,644	29,267	(43)	29,224
Equity attributable to equity holders of the parent	739,691	(1,426)	738,265	453,492	(958)	452,534	441,103	(190)	440,913
Profit (loss) per share – basic	0.25	0.09	0.34	0.22	(0.00)	0.22	(0.66)	(0.02)	(0.68)
Profit (loss) per share – diluted	0.25	0.08	0.33	0.22	(0.01)	0.21	(0.66)	(0.02)	(0.68)

<sup>1</sup> The impact of the change in the accounting policy as at January 1, 2007 is presented separately in the consolidated statements of changes in equity and the relevant notes to the financial statements.

When an entity applies an accounting policy retrospectively, IFRS requires that as a minimum, three statements of financial position, and two of each of the other statements, and related notes are presented. An entity should present the statements of financial position as at the end of the current period, the end of the previous period and as at the beginning of the earliest comparative period. Security Exchange Commission regulations require that all registrants should give two years of comparatives (to the current year) for all statements except for the statement of financial position, which requires one comparative year. Consequently the earliest comparative period presented is the statement as at the beginning of the financial year starting January 1, 2007. The Group chose not to disclose the statement of financial position as at December 31, 2007.

### 1.5.2 Accounting policies effective for the financial year 2009

The following (amendments to existing) standards and interpretations were effective for the financial year 2009.

- IFRS 8, 'Operating segments' is effective from January 1, 2009. IFRS 8 requires a 'management approach', under which segment information is presented on the same basis as that used for internal reporting purposes. The Group early adopted IFRS 8 as of January 1, 2007.
- IAS 23 (Amendment), 'Borrowing costs'. The amendment requires an entity to capitalize borrowing costs directly attributable to the acquisition, construction or production of a qualifying asset. Adoption of the amendment had no impact on the Group's financial statements as borrowing

costs directly attributable to qualifying assets are already capitalized in line with the allowed alternative treatment of IAS 23.

- IAS 1 (Revised), 'Presentation of financial statements'. The revised standard requires the presentation of items of income and expenses ('non-owner changes in equity') to be shown in a performance statement. Entities could choose to present one performance statement (the statement of comprehensive income) or two separate statements (the statement of income and statement of comprehensive income). The Group chose to present two separate statements. The revised standard also introduced a number of terminology changes, including revised titles for the statements included in the financial statements. The Group chose to adopt these terminology changes.
- IFRS 7, the amendments to IFRS 7 expand the disclosures required in respect of fair value measurements and liquidity risk. In particular, the amendment requires disclosure of fair value measurements by level of a fair value measurement hierarchy. As the change in accounting policy only results in additional disclosures, there is no impact on earnings per share.

Not all amendments to existing standards and interpretations that effective for the year 2009 have been listed above as they may not be applicable to the operations of the Group or do not have a significant impact on the financial statements of the Group.

### 1.5.3 Other new accounting pronouncements

The following amendments to existing standards and interpretations were not effective for the financial year 2009 and were not early adopted by the Group:

- IFRS 3 (Revised), 'Business combinations'. The revised standard continues to apply the acquisition method to business combinations, with some significant changes. All payments to purchase a business are to be recorded at fair value at the acquisition date, with contingent payments classified as debt subsequently re-measured through the statement of income. There is a choice on an acquisition-by-acquisition basis to measure the non-controlling interest in the acquiree either at fair value or at the non-controlling interest's proportionate share of the acquiree's net assets. All acquisition-related costs should be expensed. The Group will apply IFRS 3 (Revised) prospectively to business combinations from January 1, 2010.
- IAS 27 (revised), 'Consolidated and separate financial statements'. The revised standard requires the effects of all transactions with non-controlling interests to be recorded in equity if there is no change in control and these transactions will no longer result in goodwill or gains and losses. The standard also specifies the accounting when control is lost. Any remaining interest in the entity is remeasured to fair value, and a gain or loss is recognised in profit or loss. The Group will apply IAS 27 (revised) prospectively to transactions with non-controlling interests from January 1, 2010.
- IAS 38 (amendment), 'Intangible Assets'. The amendment is part of the IASB's annual improvements project published in April 2009 and the Group will apply IAS 38 (amendment) from the date IFRS 3 (revised) is adopted. The amendment clarifies guidance in measuring the fair value of an intangible asset acquired in a business combination and it permits the grouping of intangible assets as a single asset if each asset has similar useful economic lives. The Group will apply IFRS 38 (amendment) from 1 January 2010. The new guidance is not expected to have a material impact on the Group's financial statements.
- IFRS 5 (amendment), 'Measurement of non-current assets (or disposal groups) classified as held-for-sale'. The amendment is part of the IASB's annual improvements project published in April 2009. The amendment provides clarification that IFRS 5 specifies the disclosures required in respect of non-current assets (or disposal groups) classified as held for sale or discontinued operations. It also clarifies that the general requirements of IAS 1 still apply, particularly paragraph 15 (to achieve a fair presentation) and paragraph 125 (sources of estimation uncertainty) of IAS 1. The Group will apply IFRS 5 (amendment) from 1 January 2010. The new guidance is not expected to have a material impact on the Group's financial statements.
- IFRS 2 (amendment), 'Group cash-settled and share-based payment transactions'. In addition to incorporating IFRIC 8, 'Scope of IFRS 2', and IFRIC 11, 'IFRS 2 – Group and treasury share transactions', the amendments expand on the guidance in IFRIC 11 to address the classification of group arrangements that were not covered by that interpretation. The Group will apply IFRS 2 (amendment) from 1 January 2010. The new guidance is not expected to have a material impact on the Group's financial statements.
- IAS 39 (Amendment), 'Eligible Hedged Items'. The amendment clarifies how the principles that determine whether a risk or portion of cash flows that is eligible for designation should be applied in particular situations. The Group will apply IAS 39 (amendment) from 1 January 2010. The Group is in process of assessing the impact of the amendment on the Group's financial statements.



# Notes to the consolidated financial statements continued

Not all amendments to existing standards and interpretations that are not yet effective and not early adopted by the Group have been listed above as it is not expected that these will be included in IFRS in the foreseeable future or are not likely to have a significant impact on the financial statements of the Group.

## 2 Summary of significant accounting policies

### 2.1 Revenue recognition

#### General

In general, revenue is recognized to the extent that it is probable that the economic benefits will flow to the Group and the amount of revenue and the costs (to be) incurred in the transaction can be measured reliably. Revenue is measured at the fair value of the consideration received excluding discounts, rebates, value added taxes and duties.

Revenues are recognized on a gross basis when the Group acts as the principal in an arrangement, and recognized on a net basis when the Group acts as agent.

Goods or services traded for items of a similar nature are not regarded as transactions that generate revenue. Goods or services traded for dissimilar items are regarded as transactions that generate revenue.

#### Product sales

Revenue from product sales is recognized when:

- Significant risk and rewards of ownership of the products have passed to the buyer;
- The Group does not retain either managerial involvement to the degree usually associated with ownership or effective control over the goods sold;
- The amount of revenue and the costs (to be) incurred in the transaction can be measured reliably; and
- It is probable that the economic benefits associated with the transaction will flow to the Group.

Products could include a specific right to return, either pursuant to the sales contract or local law. Revenue from that sale is recognized at time of sale only if all of the following conditions are met in addition to the general revenue recognition terms described above:

- The customer is obligated to pay and that obligation is not contingent on resale of the product;
- The customer's obligation to pay will not be changed in the event of theft or physical destruction or damage of the product;
- The customer acquiring the product for resale has economic substance apart from that provided by the Group, e.g. the customer sells other products besides the products the Group delivers to it;
- The Group does not have significant future performance obligations to directly ensure resale of the product by the buyer; and
- The amount of future returns can be reasonably estimated.

Revenue and cost of sales that are not recognized at the time of the sale because the foregoing conditions were not met are recognized on the earlier of either the substantial expiration of the customer's right to return the product or the subsequent satisfaction of those conditions.

#### License revenues

The Group recognizes initial fees to the licensing of the technology as revenues over the period of the significant continuing performance obligations, if any, and upon transfer of the significant risks and rewards to the buyer.

Under certain arrangements, the Group has no continuing performance obligations after delivery of the associated technology under the license agreement or any other arrangement with the licensee. In such arrangements, initial license fees are recognized as revenue when significant risks and rewards pass to the buyer, which is the moment the transfer of developed technology is completed. The Group's arrangements provide for optional continuing support of its technology at standard consulting rates. Revenues derived

from aforementioned consulting services that are not essential to licensee's ability to use the Group's technology, are recognized as earned during the period that the consulting services are performed.

In certain arrangements, the Group collaborates with third parties to develop novel products or processes using its proprietary technology. These arrangements generally include an initial license fee upon the delivery of the proprietary technology and additional fees for providing ongoing research and development activities. The research and development activities performed are substantive and critical to the licensees' exploitation of the delivered technology. When significant risks and rewards pass to the buyer, initial fees from these arrangements are recognized as revenues over the period of continuing performance obligations. Additional fees from research and development activities are recognized as revenues earned over the period of the development collaboration or the manufacturing obligation. All fees received under collaboration agreements are non-refundable.

Certain of the Group's license agreements provide for additional non-refundable fees to be paid to the Group upon the achievement of milestones by the licensee. These milestone payments may be included in license agreements regardless of whether the Group has continuing performance obligations under a particular agreement.

For license agreements where there are no continuing performance obligations, milestone revenue is recognized when those amounts become due and payable upon achievement of the milestone. The licensee has to confirm the achievement of a milestone in writing before the revenue is recognized.

The Group also has license agreements with continuing performance obligations. License revenues from the achievement of these research and development milestones, if deemed substantive (as described below), are recognized as revenue when the milestones are achieved, and the milestone payments are due and collectible under the terms of the agreement.

Milestones are considered 'substantive' if all of the following conditions are met:

- The milestone payments are non-refundable under the terms of the agreement;
- Achievement of the milestone involved a degree of risk and was not reasonably assured at the inception of the arrangement;
- Substantial effort is involved in achieving the milestone;
- The amount of the milestone payment is reasonable in relation to the effort expended or the risk associated with achievement of the milestone; and
- A reasonable amount of time passed between the upfront license payment and the first milestone payment as well as between each subsequent milestone payment.

If any of these conditions are not met, the Group would recognize the proportionate amount of the milestone payment upon receipt as revenue that corresponds with the percentage of work already completed. The remaining portion of the milestone payment would be deferred and recognized as revenue as performance obligations are completed.

In addition to the initial fee, the Group's arrangements generally provide that the licensee makes semi-annual or annual payments (called 'license maintenance fees') to maintain the license for a subsequent term. Generally, licensees may terminate the license and related maintenance fees upon 30 to 90 days' notice. License maintenance fees are recognized pro rata over the duration of the license maintenance period. The aggregate of license maintenance fees paid are generally deductible from any earned royalty payments which may be due on future product sales of the licensee, if any, under the license agreement. Royalties are recognized on an accrual basis in accordance with the substance of the relevant agreement.

### Service fees

As part of various collaboration agreements, the Group receives service fees for work performed under such agreements. The Group does not retain the residual interest on products developed under the agreements and will normally not have ownership of intellectual property rights on these products. When the outcome of a transaction involving the rendering of services can be estimated reliably, revenue shall be recognized by reference to the stage of completion of the transaction. When the outcome of the transaction involving the rendering of services cannot be estimated reliably, revenue shall be recognized only to the extent of the expenses recognized that are recoverable.

# Notes to the consolidated financial statements continued

## 2.2 Cost of product sales and cost of service fees

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Cost of product sales and cost of service fees both comprise direct labor, materials and overhead costs, incurred in performing work under various collaboration agreements that directly relate to revenues earned.

## 2.3 Other operating income

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### Government grants

The Group receives certain government grants that support research efforts in defined projects. These grants generally provide for reimbursement of approved costs incurred as defined in various grants. Income associated with these grants is recognized when costs under each grant are incurred in accordance with the terms and conditions of the grant and the collectibility of the receivable is deemed probable and there is reasonable assurance that attaching conditions will be achieved. Where the grant relates to an expense item, it is recognized as income over the period necessary to match the grant on a systematic basis to the costs that it is intended to compensate.

### Other income

Other income mainly consists of the reimbursement of development costs and funding by non-governmental agencies, but also includes non-core business transactions such as the sale of property, plant and equipment and income generated from training courses.

## 2.4 Research and Development expenses

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Expenditure on research activities is recognized as an expense in the period in which it is incurred. Internally generated intangible assets arising from the Group's development activities are recognized if all of the recognition criteria for internally generated intangible assets are met, including:

- An asset is created that can be identified;
- It is probable that the asset created will generate future economic benefits; and

- The development cost of the asset can be measured reliably.

Product registration fees will, in principle, meet these recognition requirements. Where no internally generated intangible asset can be recognized, development expenditure is recognized as an expense in the period in which it is incurred. Research and development expenses consist of personnel expenses, laboratory expenses, technology purchases, patent related fees, technology license fees, depreciation and amortization of tangible and intangible assets related to research and development, and lease expenses for lab space and equipment leases. Research and development expenses also include fees paid to third parties who conduct research on behalf of the Group.

## 2.5 Taxes

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### Current tax

Current tax assets and liabilities for the current and prior periods are measured at the amount expected to be recovered from or paid to the tax authorities. The tax rates and tax laws used to compute the amount are those that are enacted, or substantively enacted, at the year-end. Current income tax relating to items recognized directly in equity is recognized in equity and not in the statement of income. Current tax assets and current tax liabilities are offset, if a legally enforceable right exists to offset the recognized amounts and the Group intends either to settle on a net basis, or to realize the asset and settle the liability simultaneously.

### Deferred tax

Deferred income tax is calculated using the asset and liability method on temporary differences at the year-end between the tax bases of assets and liabilities and their carrying amounts under IFRS. Deferred tax liabilities are recognized for all taxable temporary differences, except:

- Where the deferred tax liability arises from the initial recognition of goodwill or of an asset or liability in a transaction that is not a business combination and, at the

time of the transaction, affects neither the accounting profit nor taxable profit or loss; and

- In respect of taxable temporary differences associated with investments in subsidiaries, associates and interests in joint ventures, where the timing of the reversal of the temporary differences can be controlled and it is probable that the temporary differences will not reverse in the foreseeable future.

Deferred income tax assets are recognized for all deductible temporary differences and carry-forwards of unused tax credits and unused tax losses, to the extent that it is probable that taxable profit will be available against which the deductible temporary differences, and the carry-forwards of unused tax credits and unused tax losses, can be utilized.

The unrecognized deferred income tax assets are reassessed at each year-end and are recognized to the extent that it has become probable that future taxable profit will allow the deferred tax asset to be recovered. Deferred income tax assets and liabilities are measured at the tax rates that are expected to apply to the year when the asset is realized or the liability is settled, based on tax rates (and tax laws) that have been enacted or substantively enacted at the year-end.

Income tax relating to items recognized directly in equity is recognized in equity and not in the statement of income. Deferred tax assets and deferred tax liabilities are offset, if a legally enforceable right exists to set off current tax assets against current tax liabilities and the deferred taxes relate to the same taxable entity and the same taxation authority.

## 2.6 Profit/ (loss) per share

Basic net profit/ (loss) per share is computed based on the weighted average number of ordinary shares outstanding during the period. Diluted net profit/ (loss) per share is computed based on the weighted average number of ordinary shares outstanding, including the dilutive effect of stock options, if any.

## 2.7 Cash and cash equivalents

Cash and cash equivalents include cash in hand and all highly liquid investments with maturities of three months or less that are convertible to a known amount of cash and bear an insignificant risk of change in value.

## 2.8 Financial assets

The Group classifies its financial assets in the following categories: at fair value through profit or loss, loans and receivables, and available for sale. The Group has no held-to-maturity investments. The classification depends on the purpose for which the financial assets were acquired. Management determines the classification of its financial assets at initial recognition.

### Financial assets at fair value through profit or loss

Financial assets at fair value through profit or loss are financial assets held for trading. A financial asset is classified in this category if acquired principally for the purpose of selling in the short-term. Derivatives are also categorized as held for trading unless they are designated as formal hedges. Assets in this category are classified as current assets.

### Loans and receivables

Loans and receivables are non-derivative financial assets with fixed or determinable payments that are not quoted in an active market. They are included in current assets, except for maturities greater than 12 months after the year-end. These are classified as non-current assets. The Group's loans and receivables comprise cash and cash equivalents, trade accounts receivable, other financial assets and other current assets in the statement of financial position.

### Trade accounts receivable, other current assets and other financial assets

Trade accounts receivable, other current assets and other financial assets are recognized initially at fair value and subsequently measured at amortized cost using the effective interest method, less provision for impairment. A provision for impairment of trade receivables is established when there is objective evidence that the group will not be able to collect all amounts due according to the original terms of the receivables.

### Available-for-sale financial assets

Available-for-sale investments are those non-derivative financial assets that are designated as available-for-sale. After initial measurement, available-for-sale financial assets are measured at fair value with unrealized gains or losses being recognized directly in equity in the net unrealized gains reserve. When the investment is disposed of, the cumulative gain or loss previously recorded in equity is recognized in the statement of income. Available-for-sale investments are included in non-current assets unless

# Notes to the consolidated financial statements continued

management intends to dispose of the investment within 12 months of the year-end.

## Derecognition of financial assets

A financial asset is derecognized when:

- The rights to receive cash flows from the asset have expired;
- The Group retains the right to receive cash flows from the asset, but has assumed an obligation to pay them in full without material delay to a third party under a 'pass through' arrangement; or
- The Group has transferred its rights to receive cash flows from the asset and either has transferred substantially all the risks and rewards of the asset, or has neither transferred nor retained substantially all the risks and rewards of the asset, but has transferred control of the asset.

## 2.9 Derivative financial instruments and hedging

Derivative financial instruments are initially recognized at fair value on the date a derivative contract is entered into and are subsequently remeasured at fair value. The fair value is based on the market prices of the instruments. Derivatives are carried as assets when the fair value is positive and as liabilities when the fair value is negative. To the extent that no formal hedge accounting is applied, any gains and losses arising from changes in the fair value of the instruments are recognized in the statement of income during the period in which they arise.

The Group applies formal hedge accounting for specific forward derivative instruments that are designated as cash flow hedges. At the inception of derivative instruments, the relationship between the derivative and the underlying financial instrument, as well as the objective of the risk management and the strategy for undertaking transactions are documented. In the documentation it is also stated whether the hedge relationship is expected to be highly effective (prospective and retrospective) and how the effectiveness is tested.

Changes in the fair value of an effective derivative, that is designated and qualifies as a cash flow hedge, are recorded in equity for the effective part, until the profit or loss is affected by the variability in cash flows of the designated hedged item. The ineffective part of the cash flow hedge is recognized in the statement of income.

## 2.10 Inventories

Inventories are stated at the lower of cost or net realizable value. The cost of inventories includes expenditures for materials acquired, directly attributable costs and related production overhead expenses. Net realizable value is determined using the estimated selling price in the ordinary course of business, less estimated costs of completion and the estimated costs necessary to make the sale. Allowances are made for obsolete inventory and are included in cost of goods sold.

## 2.11 Property, plant and equipment

Property, plant and equipment is stated at cost, excluding the costs of day-to-day servicing, less accumulated depreciation and accumulated impairment in value. The cost of replacing a part of a plant or equipment is capitalized if the recognition criteria are met. Where an item of property, plant and equipment comprises major components having different useful lives, they are accounted for as separate items of property, plant and equipment. Depreciation is charged to the statement of income on a straight-line basis over the estimated useful life of the assets:

- Freehold land is not depreciated;
- Buildings: 20 to 50 years;
- Computer equipment: three years;
- Furniture and laboratory equipment: five years; and
- Leasehold improvements: the shorter of the lease term and ten years.

An item of property, plant and equipment is derecognized upon disposal or when no future economic benefits are expected from its use. Any gain or loss arising on

derecognition of the asset is included in the statement of income. The asset's residual values, useful lives and methods are reviewed, and adjusted if appropriate, at each financial year-end.

### **Borrowing costs**

Borrowing costs directly attributable to the acquisition, construction or production of qualifying assets are added to the cost of these assets until they are substantially ready for their intended use. Qualifying assets are those assets that necessarily take a substantial period of time to be completed for their intended use. All other borrowing costs are recognized as an expense in the statement of income when incurred.

### **2.12 Intangible assets**

Intangible assets acquired are measured at cost on initial recognition. The cost of intangible assets acquired in a business combination is the fair value at the date of acquisition. Following initial recognition, intangible assets are carried at cost less any accumulated amortization and accumulated impairment losses. Internally generated intangible assets are not capitalized if the recognition requirements are not met, in which case the expenses associated with generating the intangible asset are recognized in the statement of income. The useful lives of intangible assets are assessed to be either finite or indefinite. Intangible assets with finite lives are amortized over their useful lives. The amortization period and the amortization method are reviewed at least at each financial year-end. Changes in the expected useful life or the expected pattern of consumption of future economic benefits embodied in the asset are accounted for by changing the amortization period or method, and treated as changes in accounting estimates. The amortization expense on intangible assets with finite lives is recognized in the statement of income consistent with the function of the intangible asset.

The estimated useful life of the assets is as follows:

- Patents and licenses (including trademarks): one year to 20 years;
- Customer lists: three years;
- Developed technology: five years to 20 years; and
- Assets under development are not depreciated until completion of the asset.

### **2.13 Goodwill and business combinations**

Business combinations are accounted for using the purchase method. This involves recognizing identifiable assets (including previously unrecognized intangible assets) and liabilities (including contingent liabilities, but excluding future restructuring) of the acquired business at fair value.

Goodwill is measured as the excess of the total consideration over the net of the acquisition-date amounts of the identifiable assets acquired and the liabilities assumed. Goodwill includes intangible assets acquired in a business combination, which were not identifiable because the assets were either not separable or did not arise from contractual or legal rights. Goodwill recognized can significantly affect operating results of both current and future periods as goodwill is subject to an annual impairment review and not to periodic amortization.

Goodwill and fair value adjustments arising on the acquisition of a foreign operation are treated as assets and liabilities of the foreign operation and, if necessary, translated into Euro at the rate of exchange ruling at the year-end.

### **2.14 Impairment of non-financial assets**

The Group assesses non-financial assets at each reporting date to determine whether there is an indication that an asset may be impaired. If any such indication exists, or when annual impairment testing for an asset is required, the Group estimates the asset's recoverable amount. An asset's recoverable amount is the higher of the asset's fair value less costs to sell and its value in use. The recoverable amount is determined for an individual asset, unless the asset does not generate cash inflows that are largely independent of those from other assets or groups of assets. Where the carrying amount of an asset exceeds its recoverable amount, the asset is considered impaired and is written down to its recoverable amount.

An impairment loss recognized in prior periods for an asset other than goodwill shall be reversed if, and only if, there has been a change in the estimates used to determine the asset's recoverable amount since the last impairment loss was recognized. If this is the case, the carrying amount of the asset shall be increased to its recoverable amount, but



## Notes to the consolidated financial statements continued

so that the increased carrying amount does not exceed the carrying amount that would have been determined had no impairment loss been recognized for the asset in prior years.

Goodwill is reviewed for impairment annually or more frequently if events or changes in circumstances indicate that the carrying value may be impaired. Impairment is determined for goodwill by assessing the recoverable amount of the cash-generating unit to which the goodwill has been allocated. Where the recoverable amount of the cash-generating unit is less than the carrying amount of the cash-generating unit to which goodwill has been allocated, an impairment loss is recognized. Impairment losses relating to goodwill cannot be reversed in future periods.

### 2.15 Employee benefits

#### Pensions

The Group operates both defined benefit plans and defined contribution plans. For defined contribution plans, obligations for contributions are recognized as an expense when they are due. The Group has no obligation to pay further contributions into a defined contribution plan if the fund does not hold sufficient assets to pay all plan benefits.

Under defined benefit plans, the pension entitlements are calculated using the projected unit credit actuarial method. The pension liability recognized in the statement of financial position is the present value of the defined benefit obligation at the end of the financial year, less the fair value of the plan assets after adding or subtracting any unrecognized past-service costs.

The defined benefit obligation is calculated separately for each plan by estimating the amount of future benefit that employees have earned in return for their service in the current and prior periods. The defined benefit obligation benefit is discounted to determine its present value and any unrecognized past-service costs and the fair value of any plan assets are deducted. For each plan the recognized assets are limited to the net total of any cumulative unrecognized past-service costs and the present value of any future

refunds from the plan or reductions in future contributions to the plan (the 'asset ceiling'). The economic benefit available as a reduction in future contributions is determined as the present value of the estimated future service cost in each year less the estimated minimum funding contributions required in respect of the future accrual of benefits in that year. All actuarial gains and losses are recognized in the period in which they occur as a component of other comprehensive income.

#### Share-based payment transactions

##### Stock option plans

The Group operates a number of equity-settled, share-based compensation plans, under which the Group receives services from employees as consideration for equity instruments (options) of the Group. The cost of equity-settled transactions with employees is measured by reference to the fair value at the date on which the options are granted. The maximum amount to be expensed is determined by reference to the fair value of the options granted, excluding the impact of any non-market service and performance vesting conditions. The impact of market conditions on the fair value of options under these plans is estimated on the date of grant using a lattice-based option valuation model. The model calculates the likelihood of achievement of the market-based measures at various levels.

Non-market vesting conditions are included in assumptions about the number of options that are expected to vest. The cost of equity-settled transactions is recognized, together with a corresponding increase in equity, over the period in which the performance and/or service conditions are fulfilled, ending on the date on which the relevant employees become fully entitled to the award ('the vesting date'). The cumulative expense recognized for equity-settled transactions at each reporting date until the vesting date reflects the extent to which the vesting period has expired and the Group's best estimate of the number of equity instruments that will ultimately vest. The statement of income charge or credit for a period represents the movement in cumulative expense recognized as at the beginning and end of that period with the offsetting entry recorded in share premium in equity.

Every option that is exercised results in the issuance of one ordinary share.

At each end of the financial year, the estimates of the number of options that are expected to vest based on the non-marketing vesting conditions are revised. The Group recognizes the impact of the revision to original estimates, if any, in the statement of income, with a corresponding adjustment to equity.

### Share-based incentive plans

The fair value of share grants is estimated on the date of grant by multiplying the number of shares available to be granted by the fair value of the Company's shares on the grant date.

### Options granted to non-employees

The cost of options granted to non-employees is recognized at the fair value of the goods or services received, together with a corresponding increase in equity, unless that fair value of the goods or services received cannot be estimated reliably, in which case the fair value is measured by reference to the fair value of the equity instruments granted.

## 2.16 Interest-bearing loans and borrowings

Short-term financial liabilities consist of all liabilities with maturities up to one year. Long-term financial liabilities are liabilities with maturities over one year. All loans and borrowings are initially recognized at the fair value of the consideration received less directly attributable transaction costs. After initial recognition, interest-bearing loans and borrowings are subsequently measured at amortized cost using the effective interest method. Gains and losses are recognized in the statement of income when the liabilities are derecognized as well as through the amortization process. A financial liability is derecognized when the obligation underlying the liability is discharged, cancelled or expired.

## 2.17 Provisions

Provisions are recognized when there is a present obligation (legal or constructive) as a result of a past event, it is probable that an outflow of resources embodying economic benefits will be required to settle the obligation and a reliable estimate of the obligation can be made. The expense relating to any provision is presented in the statement of income net of any reimbursement. If the effect of the time

value of money is significant, provisions are discounted. Where discounting is used, the increase in the provision due to the passage of time is recognized as a financial expense.

## 2.18 Leases

Leases of property, plant and equipment where the Group assumes substantially all the risks and rewards of ownership of the leased asset are classified as finance leases. Finance leases are capitalized at the inception of the lease at the fair value of the leased property or, if lower, at the present value of the minimum lease payments. Lease payments are apportioned between the finance charges and reduction of the lease liability to achieve a constant rate of interest on the remaining balance of the liability. Finance charges are charged directly against income. Capitalized leased assets are depreciated over the shorter of the estimated useful life of the asset or, over the lease term, if there is no reasonable certainty that the Group will own the leased property by the end of the lease term.

Leases where the Group does not assume substantially all the risks and rewards of ownership are classified as operating leases, and are recognized as an expense in the statement of income on a straight-line basis over the lease term.

The determination of whether an arrangement is, or contains, a lease is based on the substance of the arrangement and requires an assessment of whether the fulfillment of the arrangement is dependent on the use of a specific asset or assets and the arrangement conveys a right to use the asset.

## 3 Financial risk management

### 3.1 Risk management policies

The Group's activities expose it to a variety of financial risks: market risk (including currency risk, interest rate risk and security price risk), credit risk and liquidity risk. These risks are discussed in note 3.2 to 3.6. The Group's overall financial risk management seeks to minimize potential adverse effects resulting from the unpredictability of financial markets on the Group's financial performance.

The goals of the Group's financial risk management are described in the treasury policies. The adherence to these policies is monitored by corporate treasury. The goals of the Group's corporate treasury function are to reduce the currency exposures in the statement of income,

## Notes to the consolidated financial statements continued

optimize return on investments in cash deposits, provide financing services to the business and monitor the Group's financial risks.

The Group has specific operating procedures that prescribe the working practice on relevant specific financial risk management topics such as use of derivative financial instruments, investment of excess liquidity, centralization of cash, statement of financial position forecast procedures and authorization levels.

The Group uses derivative financial instruments to hedge certain foreign currency risk exposures. Corporate treasury is responsible for using derivatives to mitigate foreign exchange risk arising from anticipated transactions and recognized monetary positions. Corporate treasury does this in close co-operation with the Group's subsidiaries. Since 2008, the Group adopted a more proactive approach in hedging foreign currency exposures on monetary positions and forecasted transactions. In 2008, the Group applied for the first time formal hedge accounting to address specific economic exposures.

### Capital risk management

The Group manages its capital to ensure that it will be able to continue as a going concern. The Group does not have a target debt-to-equity ratio. Although the Group entered into finance leases and loans in the past, the Group is committed to funding the majority of its operations with equity. The Group may choose to renew any loan that becomes payable.

The capital structure of the Group consists of financial liabilities and equity attributable to equity holders of the parent, comprising issued capital, reserves and retained earnings.

Financial liabilities compared to total equity	December 31, 2009	December 31, 2008	January 1, 2007
Total financial liabilities	52,300	61,630	46,413
Total equity	738,265	452,534	497,683
<b>Equity / financial liabilities</b>	<b>14.1</b>	<b>7.3</b>	<b>10.7</b>

The equity/ financial liabilities ratio improved significantly as a result of the JNJ 18% equity investment.

### Working Capital Management

The Group tries to minimize investment in working capital, without jeopardizing the Group's commercial objectives.

In specific cases, the Group may chose to enter into factoring arrangements to manage the cash flow on outstanding trade accounts receivable. The Group did not engage in factoring arrangements in 2009.

In 2008, the Group entered into factoring arrangements relating to certain Italian customers that allowed derecognition of accounts receivable in an amount of € 11,107. In 2008, the Group also entered into factoring arrangements with a third party to sell a portion of its receivables in an amount of € 14,886 from product sales made during the month of December to a supranational organization. Consequently accounts receivables outstanding from this customer were relatively low as at the end of financial year 2008.

As part of the overall working capital management efforts, the Group agreed with Novartis in 2008 to extend payment terms on the supply of Quinvaxem antigens. We have provided Novartis with collateral on our Swiss premises for an amount up to € 30,254. These payment terms still apply in 2009.

### Significant accounting policies

Details of the significant accounting policies and methods adopted, including the criteria for recognition, the basis of measurement and the basis on which income and expenses are recognized, in respect of each class of financial asset, financial liability and equity instrument are disclosed in note 2.

### 3.2 Foreign currency risk

The Group divides the foreign currency risk into categories of transaction exposure, economic exposure and translation exposure.

The Group defines transaction exposure as the foreign currency exposure arising on monetary positions and forecasted transactions in the coming month that are denominated in a currency other than the functional currency of the group company. The Group has significant transactional currency exposures as the majority of the Group's sales are denominated in currencies other than the functional currency of the reporting subsidiaries. Specifically, movements in the US Dollar/ Euro exchange rate affect the results of operations because a significant portion of sales are denominated in US Dollars. The Group's operating procedures require group companies to manage the foreign exchange risks against their functional currency. The target is to minimize foreign currency results on monetary items in the statement of financial position. Corporate treasury may hedge any remaining foreign exchange risk exposure on monetary items.

The Group defines economic exposure as the foreign currency exposure to which the Group committed itself. This is the exposure associated with the time delay between entering into a contract, budget or forecast and the realization thereof. It is not the Group's policy to actively manage these exposures, but rather to hedge economic exposure on a selective basis by Management's decision. The Group may apply formal hedge accounting in mitigating these risks. The Group is currently investigating whether it will adopt a more proactive approach to cover economic exposures.

The translation exposure is the exposure that arises on the translation of the financial statements of subsidiaries with different functional currencies into Euro. The Group has operations in Switzerland, Korea, Sweden, the UK and the US, which all have a different functional currency than the Euro. Consequently, movements in the currencies of these countries against the Euro will affect the results of operations because the statement of financial position and the statement of income of these subsidiaries are translated into Euro. The Group does not actively hedge its translation exposure.

#### Foreign currency risk sensitivity analysis

The Group is mainly exposed to US Dollar, Swiss Franc, Korean Won, Swedish Crown and Australian Dollar. The following table details the Group's sensitivity to a 10% strengthening of these currencies. The sensitivity analysis includes outstanding foreign currency denominated monetary items and adjusts their translation as at December 31, 2009 for a 10% change in foreign currency rates. A positive amount indicates an increase in income before income tax and equity.

For a 10% weakening of the foreign currencies against the Euro, there would be approximately an equal and opposite effect on the income before income tax and equity. The revaluation effects of investments in foreign entities are recognized in equity. As we have significant operations denominated in other currencies than the Euro, the movements of currency exchange rates show a significant effect on equity. It is the Group's policy to limit the currency effects reported in financial income and expenses. The Group does not proactively manage the currency exposure on the Group's equity.

	2009		2008		2007
	Impact on statement of income	Impact on equity	Impact on statement of income	Impact on equity	Impact on statement of income
US Dollar	754	419	229	482	1,876
Swiss Franc	(1,624)	18,945	(373)	17,980	(4,950)
Korean Won	(755)	17,521	(133)	8,414	860
Swedish Crown	(424)	2,797	(538)	2,924	(486)
Australian dollar	5	436	5	808	882

# Notes to the consolidated financial statements continued

## 3.3 Interest rate risk

The Group is exposed to interest rate risks as a result of changes in the market interest rates compared to loans with fixed rates. The Group has several loans with fixed interest rates, which total € 34,018 (2008: € 39,896). The Group has financial liabilities of € 17,988 with a variable interest rate as at December 31, 2009 (2008: € 20,855). Details on the interest rates and maturity of these loans are provided in note 5.20 'Short and long-term financial liabilities'.

The Group owns financial assets that generate interest in an amount of € 440,860 (2008: € 183,865).

### Interest rate risk sensitivity analysis

The sensitivity analysis has been determined based on the exposure to interest rates at the year-end and the stipulated change taking place at the beginning of the financial year and held constant throughout the reporting period. The effect of a 1% increase in interest rates on the Group's profit/ (loss) before tax would be a positive result of € 3,522 (2008: € 947; 2007: € 1,100). If the interest rates decrease by 1% the impact on the profit/ (loss) before tax would be a negative result of € 1,689 (2008: € 947). A change in the interest rate does not have an impact on the equity of the Group.

The positive effects of a 1% increase or decrease of interest on profit/ (loss) before tax is mainly attributable to the Group's interest income generating assets, which are higher than the financial liabilities.

## 3.4 Credit risk

Credit risk represents the risk of financial loss caused by default of the counterparty. The Group's principal financial assets are cash and cash equivalents, short-term deposits and trade and other receivables. These represent the Group's maximum exposure to credit risk in relation to financial assets.

The Group's credit risk is primarily attributable to its trade accounts receivable and other receivables. The Group

normally trades only with recognized, credit-worthy third parties. It is the Group's policy that all customers who wish to trade on credit terms are subject to credit verification procedures. Where considered appropriate, the Group requires issuance of letters of credit to mitigate credit risk.

Receivable balances are monitored on an ongoing basis and the Group tracks the payment history of its customers to identify any payment issues that have to be resolved before entering into any new transactions. Allowances are recognized for receivable balances deemed uncollectible upon identification. In determining the recoverability of a trade receivable, the Group considers changes in the credit quality of the trade receivable from the date credit was initially granted up to the reporting date. The customer base consists mainly of well-respected companies in the field of medicine and non-governmental organizations. In 2009, the Group has not encountered significant adverse events as a result of the weak global economy. While the Group does have concentrations of trade accounts receivable outstanding to supranational organizations, management has determined the risk of default by these organizations to be limited and therefore considers the credit risk to be within acceptable boundaries. Management believes that no further credit provision is required in excess of the allowance for doubtful debts. As at December 31, 2009 an amount of € 22,122 trade accounts receivable were outstanding to these supranational organizations.

The credit risk is dispersed as cash and cash equivalents and short-term deposits are placed with numerous major financial institutions. Furthermore the Group currently only invests in current securities and money market transactions. Management does not expect any counterparty to fail to meet its obligations.

The carrying value of these financial assets represents the Group's maximum exposure to credit risk. The maximum exposure at December 31, 2009 amounted to € 552,526 (2008: € 242,206). See note 5.24 'Financial instruments- Financial assets' for more information on the categorization of the financial assets.

### 3.5 Security price risk

The Group's security price risk is predominantly limited to its investment in Galapagos, a biopharmaceutical company listed on NYSE Euronext, valued at € 10,136 (2008: € 4,922). The investment is classified as an available-for-sale investment. The fair value is based on the market quotation of Galapagos. The Group does not actively trade in available-for-sale investments.

#### Security price risk sensitivity analysis

The sensitivity analysis below has been determined based on the exposure to the security price risks at the reporting date. If the Galapagos share price had been 10% higher/lower:

- The profit for the year ended 31 December 2009 would have been unaffected as the investments are classified as available-for-sale and no investments were disposed of or impaired; and
- Net unrealized gains reserve would increase/decrease by € 1,044 (2008: increase/decrease by € 492) for the Group as a result of the changes in the fair value of the available-for-sale investment.

The Group's sensitivity to security prices did not change significantly from the prior year.

### 3.6 Liquidity risk

Liquidity risk represents the risk that an entity will encounter difficulty in meeting obligations associated with its financial liabilities. Prudent liquidity risk management implies ensuring sufficient availability of cash resources for funding of the operations. The Group aims to maintain a solid cash base.

Some of the Group's arrangements with financial institutions are subject to covenant clauses, whereby the Group is required to maintain certain cash thresholds. The Group did not breach any of these covenant clauses in 2009 nor does the Group foresee any breaches of these covenants in the foreseeable future.

The current liquidity risk is considered to be limited because the Group has sufficient funding to meet its obligations in the foreseeable future. Reference is made to note 5.20 'Short and long-term financial liabilities' for an analysis of the most significant financial liabilities.

## 4 Segment information

### 4.1 General

The Group operates in one reportable segment, which comprises the development, production and marketing of products that combat infectious diseases. The Group identified the Management Board as the 'chief operating decision maker'. The Management Board reviews the consolidated operating results regularly to make decisions about resources and to assess overall performance.

### 4.2 Information about major products

The breakdown of the Group's revenues from its product sales was as follows:

In thousands of Euro

Year ended December 31,	2009	2008	2007
Paediatric vaccines	<b>180,389</b>	111,039	77,371
Respiratory vaccines	<b>38,070</b>	32,474	33,188
Travel and endemic vaccines	<b>53,078</b>	55,572	47,282
Other vaccines	<b>8,391</b>	8,907	10,705
Proteins and other business	<b>24,511</b>	18,063	9,023
	<b>304,439</b>	<b>226,055</b>	<b>177,569</b>

### 4.3 Information about major customers

In 2009, sales to our two largest customers, which are in the paediatric vaccines area, amounted to € 148,072 or 48.6% and € 21,013 or 6.9% of net product sales. In 2008, sales to these customers accounted for € 85,142 or 37.6% and € 18,390 or 8.1% of net product sales, respectively.



# Notes to the consolidated financial statements continued

## 4.4 Geographical segments

The Group operates principally in three geographical areas: Europe, North America and Asia. Segment revenue is based on the geographical location of the customers, which is the billing location of the customers. Segmentation of the assets is based on the geographical location of the assets.

Domestic product sales amount to € 3,553 or 1.2% (2008: € 3,743 or 1.7% and 2007: € 717 or 0.4%). Almost all of our license revenues and service fees are billed to foreign parties.

In thousands of Euro

Year ended December 31,	2009	2008	2007
<b>Revenue</b>			
Europe	262,240	209,473	144,969
North America	39,565	33,653	33,346
Asia	31,994	19,095	18,589
Other	4,364	4,936	6,882
<b>Total</b>	<b>338,163</b>	<b>267,157</b>	<b>203,786</b>

In thousands of Euro

Year ended December 31,	2009	2008
<b>Non-current assets as defined in IFRS 8</b>		
The Netherlands	91,970	83,859
Europe	137,136	142,442
North America	5,558	5,190
Asia	91,606	54,034
<b>Total</b>	<b>326,270</b>	<b>285,525</b>

In thousands of Euro

Year ended December 31,	2009	2008
<b>Total assets</b>		
The Netherlands	467,558	194,967
Europe	312,680	303,225
North America	7,753	7,472
Asia	223,140	130,633
<b>Total</b>	<b>1,011,131</b>	<b>636,297</b>

## 5 Notes to the specific items of the consolidated financial statements

### 5.1 Personnel expenses

In thousands of Euro

	2009	2008	2007
Wages and salaries	66,538	59,634	58,493
Social security costs	7,020	6,806	6,734
Pension defined benefit plans	(73)	254	220
Pension defined contribution plans	2,241	2,410	2,436
Cost of share-based payments	7,511	4,878	7,349
Other personnel expenses	6,636	6,436	9,810
	<b>89,873</b>	<b>80,418</b>	<b>85,042</b>

As of December 31, 2009, the Group had 1,248 employees (2008: 1,126). The average number of employees in 2009 was 1,188 (2008: 1,142). Personnel as at December 31, 2009 are employed in the following categories:

	2009	2008	2007
Research and Development	376	303	368
General and administrative	170	147	134
Operations	521	527	466
Marketing and sale	181	149	158
<b>Total</b>	<b>1,248</b>	<b>1,126</b>	<b>1,126</b>

The Group's personnel are located primarily in the Netherlands, Switzerland, Spain, Italy, Korea, Sweden, the UK, the US and China.

The split per geographical area is as follows:

	2009	2008	2007
Europe	969	861	916
North America	19	19	19
Asia	260	246	191
<b>Total</b>	<b>1,248</b>	<b>1,126</b>	<b>1,126</b>

## 5.2 Financial income

In thousands of Euro

	2009	2008	2007
Currency gains	6,591	1,914	7,479
Interest income	2,429	5,021	5,711
	<b>9,020</b>	<b>6,935</b>	<b>13,190</b>

## 5.3 Financial expenses

	2009	2008	2007
Interest expense	<b>(3,568)</b>	(2,973)	(3,053)
Less: amounts included in the cost of qualifying assets	<b>619</b>	254	772
	<b>(2,949)</b>	(2,719)	(2,281)
Currency losses	<b>(8,915)</b>	(5,840)	(8,785)
Other financial expenses	<b>(349)</b>	(1,038)	(746)
	<b>(12,213)</b>	<b>(9,597)</b>	<b>(11,812)</b>

## 5.4 Income tax

In thousands of Euro

Year ended December 31,	2009	2008	2007
Current income tax <sup>1</sup>	<b>(10,653)</b>	(3,193)	(816)
Deferred taxation	<b>(3,375)</b>	11,595	3,414
<b>Income tax</b>	<b>(14,028)</b>	<b>8,402</b>	<b>2,598</b>

<sup>1</sup> Current income tax includes an adjustment gain of the current tax charge of previous years in an amount of € 26 (2008: € 7, 2007: € (5)).

The reconciliation between the profit/ (loss) for the year multiplied by the applicable tax rate and the actual taxation is as follows:

In thousands of Euro

Year ended December 31,	2009	2008	2007
Profit/(loss) for the year before income tax	<b>37,966</b>	5,848	(46,932)
At gross weighted average income tax rate	<b>(2,764)</b>	912	12,587
Timing differences not recognized	<b>(7,387)</b>	(6,301)	(380)
Recognition tax loss carry forwards	—	9,284	4,072
Effect of tax rate changes	<b>(211)</b>	3,527	(197)
R&D tax credit	<b>331</b>	2,916	—
Other permanent differences	<b>(1,665)</b>	(1,734)	(3,493)
Tax losses not recognized	<b>(2,332)</b>	(202)	(9,991)
Income tax	<b>(14,028)</b>	8,402	2,598
Effective income tax rate	<b>36.9%</b>	(143.7%)	5.5%

The changes in deferred income tax assets and liabilities on a net basis were as follows in 2009, 2008 and 2007:

In thousands of Euro

	2009	2008	2007
January 1,	<b>(16,644)</b>	(29,224)	(33,438)
Change in accounting policy	—	—	45
Deferred tax through statement of income	<b>(3,375)</b>	11,595	3,414
Deferred tax through goodwill	—	—	(697)
Deferred tax through equity	<b>1,786</b>	257	(388)
Effects of movements in exchange rates	<b>(389)</b>	728	1,840
December 31,	<b>(18,622)</b>	(16,644)	(29,224)

Deferred tax through equity reflects the tax impact on the actuarial gains and losses on pensions that are directly recognized in other comprehensive income.

In 2007, a deferred tax asset of € 580 was recognized against goodwill as an adjustment to the provisional purchase price allocation on the acquisition of SBL Vaccin Holding AB. A deferred tax liability of € 1,277 was recognized against goodwill as an adjustment to the provisional purchase price allocation on the acquisition of Berna Products Corp.

## Notes to the consolidated financial statements continued

The composition of the temporary differences and tax loss carry forwards in the statement of financial position is as follows:

In thousands of Euro

Year ended December 31,	2009	2008
<b>Deferred income tax liabilities</b>		
Valuation differences attributable to: Inventories	(2,555)	(2,171)
Other assets	(1,287)	(1,614)
Net pension assets	(628)	(1,852)
Property, plant and equipment	(8,542)	(7,316)
Intangible assets	(12,920)	(14,580)
Other liabilities	(1,416)	(1,649)
	(27,348)	(29,182)
<b>Deferred income tax assets</b>		
Losses available for offset against future taxable income	5,488	9,060
Valuation differences attributable to: Inventories	579	469
Other assets	542	1,273
Property, plant and equipment	1,775	1,202
Other liabilities	342	534
	8,726	12,538
Offset of deferred tax balances	8,518	12,538
Reflected in the statement of financial position as follows:		
Deferred tax assets	208	—
Deferred tax liability	(18,830)	(16,644)
Deferred tax liabilities, net	(18,622)	(16,644)

The Group has unrecognized tax carry forward losses of € 180,261 (2008: € 172,732; 2007: € 254,511) that are available, with certain restrictions in time, for offset against future taxable profits of the companies in which the losses arose. In the Netherlands anti-abuse laws may limit our ability to realize certain tax carry forward losses for an amount up to € 26,170.

In 2008, the Group agreed with the Dutch tax authorities to retrospectively change the valuation of our intellectual property for tax purposes to avoid the evaporation of unrecognized tax carry forward losses in the Netherlands. As per year-end 2009 an amount of € 90,375 of our intellectual property was recognized as intangible assets for tax purposes. These assets for tax purposes are depreciated ratably over time over a period of 20 years. The difference between tax value and IFRS value is not recognized as a deferred tax asset.

The unrecognized carry forward losses relate to the Dutch and Italian operations of the Group and expire as follows:

2010	—
2011- 2012	38,666
2013-2014	22,693
2015	40,159
After 2015	77,587
Unlimited	1,156
Total	180,261

### Tax holidays

In the years 2009 and 2008 the Group benefited from a tax holiday in Korea. The group received a discount of 40% and 37% respectively for tax payable in these years. The tax holiday was granted by the Korean tax authorities in recognition of a foreign investment in an eligible high technology business. Prior to 2007 the net benefit of the tax holiday was nil due to tax loss carry forwards. For the years 2009 and 2008 the net benefit of the tax holiday was € 5,363 and € 2,758. This tax holiday ended on December 31, 2009.

Starting in 2012, the Group will benefit from a new tax holiday in Korea. This tax holiday was granted in 2008 following the Group's commitment to make a direct foreign investment in the share capital of the Korean subsidiary. The investment was made in an amount equal to \$ 30 million and was used for the new production facility in the Incheon Free Economic Zone. Based upon the ratio between new share capital and existing share capital, a reduction of 76% is granted on the nominal tax amount payable for the years 2012-2016. For the years 2017 and 2018 the reduction is 38% on the nominal tax amount payable. As per the end of 2009 the deferred tax liabilities in the statement of financial position were € 2,083 lower compared to if no tax holiday had been granted to the Group.

### Tax rate changes

In financial year 2009, the applicable tax rate in Korea was 16.5%. As of 2010 the tax rate will be the nominal income tax rate of 24% as the current tax holiday ended December 31, 2009.

The Swedish domestic statutory corporate income tax rate amounted to 28.0% in 2008 and changed to 26.3% in 2009 and the years thereafter.

## 5.5 Profit/ (loss) per share

In thousands of Euro, except per share data			
Year ended December 31,			
	2009	2008	2007
Profit/ (loss) attributable to ordinary shareholders	<b>23,938</b>	14,250	(44,334)
Weighted average number of ordinary shares for the year	<b>70,265,644</b>	65,593,374	65,102,801
Dilutive effect share options	<b>1,419,673</b>	721,682	—
Weighted average number of ordinary shares including dilutive effect	<b>71,685,317</b>	66,315,056	65,102,801
Net profit / (loss) per share—basic	<b>0.34</b>	0.22	(0.68)
Net profit / (loss) per share—diluted	<b>0.33</b>	0.21	(0.68)

# Notes to the consolidated financial statements continued

## 5.6 Property, plant and equipment

Amounts in thousands of Euro

	Freehold Land and buildings	Plant and equipment	Assets under construction	Total
<b>Cost At January 1, 2008</b>	<b>65,607</b>	<b>74,709</b>	<b>54,884</b>	<b>195,200</b>
Additions	66	7,917	7,804	15,787
Disposals	—	(1,444)	—	(1,444)
Transfer assets under construction	66	35,204	(35,270)	—
Disposal of subsidiary	—	(176)	—	(176)
Effect of movements in exchange rates	5,456	2,450	1,886	9,792
<b>At December 31, 2008</b>	<b>71,195</b>	<b>118,660</b>	<b>29,304</b>	<b>219,159</b>
Additions	319	11,237	39,479	51,035
Disposals	(13)	(4,676)	—	(4,689)
Transfer assets under construction	5,758	252	(6,010)	—
Effect of movements in exchange rates	1,010	2,170	2,268	5,448
<b>At December 31, 2009</b>	<b>78,269</b>	<b>127,643</b>	<b>65,041</b>	<b>270,953</b>

### Depreciation and impairment

<b>At January 1, 2008</b>	<b>(14,778)</b>	<b>(34,897)</b>	<b>—</b>	<b>(49,675)</b>
Depreciation charge for the year	(6,715)	(9,914)	—	(16,629)
Reversal of Impairment/ (impairment)	4,953	(65)	—	4,888
Disposals	—	1,444	—	1,444
Disposal of subsidiary	—	54	—	54
Effect of movements in exchange rates	(3,526)	(4,509)	—	(8,035)
<b>At December 31, 2008</b>	<b>(20,066)</b>	<b>(47,887)</b>	<b>—</b>	<b>(67,953)</b>
Depreciation charge for the year	(9,154)	(11,239)	—	(20,393)
Impairment	—	(565)	(320)	(885)
Reversal of impairment	3,827	4,257	—	8,084
Disposals	13	4,378	(143)	4,248
Effect of movements in exchange rates	(607)	(837)	5	(1,439)
<b>At December 31, 2009</b>	<b>(25,987)</b>	<b>(51,893)</b>	<b>(458)</b>	<b>(78,338)</b>

### Net book value

<b>At December 31, 2009</b>	<b>52,282</b>	<b>75,750</b>	<b>64,583</b>	<b>192,615</b>
<b>At December 31, 2008</b>	<b>51,129</b>	<b>70,773</b>	<b>29,304</b>	<b>151,206</b>

Depreciation is included in the cost of goods sold for an amount of € 12,094 in 2009 (2008: € 10,026; 2007: € 11,176), research and development costs of € 5,770 in 2009 (2008: € 4,157; 2007: € 2,353) and selling, general and administrative costs of € 2,529 in 2009 (2008: € 2,446; 2007: € 924).

### Impairment

See note 1.4 'Use of estimates and judgments' in the financial statements for further details on any impairments or reversal thereof.

### Useful lives

The Group reviews the estimated useful lives of property, plant and equipment at the end of each annual reporting period. In 2009, Management determined that in Korea, the useful lives of certain items of property, plant and equipment from the Shingal site can only be used until the moment of the relocation to new Incheon site. As a result the useful life of these assets was reduced to reflect that the asset will be fully depreciated by March 31, 2011. The assets are subject to accelerated depreciation, which leads to a higher depreciation charge in the coming periods. In 2009, the impact on the profit before tax was an additional charge of € 806.

### Lease and borrowing costs

At December 31, 2009 and 2008, the Group held equipment under finance leases with a cost of € 23,568 and € 23,505, respectively, and a net book value of € 19,727 and € 21,936, respectively. The equipment under finance leases includes the new Spanish filling line and laboratory equipment in Leiden, the Netherlands. These leases are secured by the value of the underlying assets.

At December 31, 2009 an amount of € 619 of borrowing costs related to the construction of the new production facility in Korea were capitalized. The borrowing costs are capitalized at an average capitalization rate of 5.25%. The borrowing cost in 2008 of € 254 related to the new production facility in Leiden, the Netherlands.

### Commitments

The remaining contractual commitments amount to € 15,755 (2008: € 20,380; 2007: € 4,696) for purchases of property, plant and equipment, mainly related to the new Korean production facility in the Incheon, Free Economic Zone, Korea.

## 5.7 Intangible assets

In thousands of Euro

Cost	Customer lists	Patents and licenses	Developed technologies	Assets under development	Total
<b>At January 1, 2008</b>	<b>10,870</b>	<b>22,314</b>	<b>80,836</b>	<b>6,757</b>	<b>120,777</b>
Effect of movements in exchange rates	1,172	2,480	(6,384)	770	(1,962)
<b>At December 31, 2008</b>	<b>12,042</b>	<b>24,794</b>	<b>74,452</b>	<b>7,527</b>	<b>118,815</b>
Additions	—	—	324	4,986	5,310
Acquisition of subsidiaries	448	—	—	—	448
Effect of movements in exchange rates	15	91	2,193	4	2,303
<b>At December 31, 2009</b>	<b>12,505</b>	<b>24,885</b>	<b>76,969</b>	<b>12,517</b>	<b>126,876</b>

### Amortization

<b>At January 1, 2008</b>	<b>(3,957)</b>	<b>(6,683)</b>	<b>(16,092)</b>	<b>—</b>	<b>(26,732)</b>
Amortization	(3,141)	(3,706)	(4,827)	—	(11,674)
Effect of movements in exchange rates	(640)	(1,299)	534	—	(1,405)
<b>At December 31, 2008</b>	<b>(7,738)</b>	<b>(11,688)</b>	<b>(20,385)</b>	<b>—</b>	<b>(39,811)</b>
Amortization	(2,594)	(4,491)	(4,022)	—	(11,107)
Effect of movements in exchange rates	(32)	(85)	(443)	—	(560)
<b>At December 31, 2009</b>	<b>(10,364)</b>	<b>(16,264)</b>	<b>(24,850)</b>	<b>—</b>	<b>(51,478)</b>

### Net book value

<b>At December 31, 2009</b>	<b>2,141</b>	<b>8,621</b>	<b>52,119</b>	<b>12,517</b>	<b>75,398</b>
<b>At December 31, 2008</b>	<b>4,304</b>	<b>13,106</b>	<b>54,067</b>	<b>7,527</b>	<b>79,004</b>



## Notes to the consolidated financial statements continued

Amortization of intangible assets is included in the cost of goods sold for an amount of € 114 in 2009 (2008: € 127; 2007: € 131), research and development costs of € 8,248 in 2009 (2008: € 8,635; 2007: € 8,939) and selling, general and administrative costs of € 2,745 in 2009 (2008: € 2,912; 2007: € 2,824).

### Useful lives

The Group reviews the estimated useful lives of intangible assets at the end of each annual reporting period. In November 2009, the Group announced the launch of the global Crucell brand, a consistent identity for its worldwide activities and products. As a result of the global rebranding, the useful life of the trademarks of Berna Biotech and SBL was reduced to a maximum of 3 years as these trademarks are gradually phased out. The impact in 2009 on the profit before tax was an additional charge of € 597.

### Material intangible assets

The following individual intangible assets are considered material to the Group's financial statements:

In thousands of Euro

	Remaining amortization at December 31, 2009 (in years)	Carrying value December 31, 2009	Carrying value December 31, 2008
Developed technology Quinvaxem	<b>16.7</b>	25,610	25,519
Developed technology Epaxal	<b>16.2</b>	10,325	10,959
Developed technology Inflexal	<b>8.2</b>	6,314	7,084
In-process R&D Flavimun	—	7,530	7,526
Developed Technology Vivotif	<b>16.2</b>	5,271	5,595

## 5.8 Goodwill and business combinations

### 5.8.1 Goodwill

Goodwill is measured as the excess of the total consideration over the net of the acquisition-date amounts of the identifiable assets acquired and the liabilities assumed. Goodwill includes intangible assets acquired in a business combination, which were not identifiable because the assets were either not separable or did not arise from contractual or legal rights. Goodwill recognized can significantly affect operating results of both current and future periods as goodwill is subject to an annual impairment review and not to periodic amortization.

In thousands of Euro

	Goodwill
<b>Cost</b>	
<b>At January 1, 2008</b>	<b>44,377</b>
Adjustment to cost of business combination	237
Effect of movements in exchange rates	1,462
<b>At December 31, 2008</b>	<b>46,076</b>
Adjustment to cost of business combination	167
Effect of movements in exchange rates	581
<b>At December 31, 2009</b>	<b>46,824</b>
<b>Net book value</b>	
<b>At December 31, 2009</b>	<b>46,824</b>
<b>At December 31, 2008</b>	<b>46,076</b>

The selling shareholders of SBL Vaccin acquisition Holding AB are contractually entitled to earn-out payments based on contingent future events. Additional consideration resulting from the earn-out agreement with the former shareholders was treated as an adjustment to the cost of the business combination for an amount of € 167 and € 237 in 2009 and 2008, respectively. This contingent consideration was not recognized in the prior year because the amount could not be measured reliably.

The goodwill has fully been allocated to the businesses that were acquired in 2006 as a single cash generating unit.

- In February 2006, the Company acquired approximately 97% of the outstanding common shares of Berna Biotech AG ('Berna Biotech') for € 348,852, excluding acquisition costs. During 2006 the remaining outstanding shares were also acquired. Berna Biotech was a fully integrated biotechnology company that marketed numerous vaccines on a global scale.
- In October 2006, the Group purchased, via its subsidiary Crucell Vaccines Inc. the assets and liabilities of the Florida-based Berna Products Corp. ('BPC') from Acambis plc for € 13,806. BPC was originally established in 1990 by Berna Biotech to market Vivotif, Berna's oral typhoid fever vaccine, in the US and Canada.
- In November 2006, the Group acquired, via its subsidiary Crucell Holland B.V. the shares of Stockholm-based SBL Vaccin Holding AB (SBL) from 3i and SEB for a total consideration of € 39,341 in cash. SBL's main product was Dukoral. In addition, SBL has a sales and distribution organization for vaccines in Scandinavia.

### Impairment testing methodology and key assumptions

The CGU's recoverable amount is based on the fair value less costs to sell. Given that due to the level of specificity of the CGU no observable market price exists, the fair values less costs to sell is based on discounted net present value calculations that use assumptions applicable in the current market as well as management's past experience about the key assumptions.

The valuation is based on a discounted future cash flow model based on the Group's latest long range plans which have been benchmarked to external market information. The Group's long range plans use a 5-year planning horizon.

## Notes to the consolidated financial statements continued

The key assumptions used in the cash flow projections are the growth rate after the 5-year planning horizon, the level of research and development expenses incurred to guarantee future products, and the weighted average cost of capital (WACC).

The recoverable goodwill amount was determined on the basis of a (pre-tax) discount rate of 13.0%, a growth rate after the 5-year planning horizon of 0% and research and development expenditures as a percentage of sales of 15%.

Calculations of the recoverable amount show that there is no impairment as the recoverable amount of the 2006 business acquisitions exceeds the carrying amount of € 265 million (2008: € 235 million) by € 146 million (2008: € 189 million).

Management believes that any reasonable possible change in the key assumptions would not decrease the recoverable amount to the extent that the related carrying amount would exceed the recoverable amount. Several sensitivity analyses on key assumptions were performed and the outcome indicated that the carrying amount would not exceed the recoverable amount.

### 5.8.2 Acquisition selected assets and liabilities of Masta Ltd.

On June 5, 2009 the Group established Crucell UK Ltd. On July 15, 2009 the Group purchased, via its subsidiary Crucell UK Ltd. selected assets and liabilities of UK-Based Masta for an amount of £ 105. The relevant assets acquired pertain to the customer base and the workforce of the UK fields activities of Masta Ltd. In addition, Masta Ltd received monthly payments from March 1, 2009 to July 1, 2009 for a total amount of £ 304 from the Group as consideration for pre-acquisition costs directly related to the business combination.

The Group recognized the identifiable assets acquired and the liabilities assumed at their respective fair values. The consideration allocated to the acquired customer contracts amounted to £ 405. No goodwill was recognized in the business combination. Based on the magnitude of the business combination, not all specific disclosures as required by IFRS 3 were included.

## 5.9 Investments in associate and joint venture

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### 5.9.1 Associated company

#### ADImmune Corp., Taiwan

The Group has an 11.8% stake in the share capital of Taiwan-based ADImmune Corp., (ADImmune) a company that develops, manufactures and distributes vaccines and other biopharmaceutical products. During 2008, our ownership of ADImmune Corp. was diluted from 20% to 11.8%. ADImmune obtained a license to the Group's virosome technology to produce a virosome adjuvanted influenza vaccine for the following markets: Taiwan, Japan and Macau. Additionally, ADImmune will produce influenza antigen in the future, which we may purchase to produce our influenza vaccine product, Inflexal V.

Although the Group holds less than 20% of the outstanding share capital, ADImmune is accounted for as an associate. The Group concludes it has significant influence over ADImmune as the Group has a seat in the governing body of ADImmune.

Summary financial information of ADImmune (unaudited) for the years ended December 31, 2009, not adjusted for the percentage of ownership held by the Group, is as follows:

In thousands of Euro

ADImmune Corp.	As of December 31,		Year ended December 31,		
	Total assets	Total liabilities	Revenues	Expenses	Profit/ (loss) before tax
2009	127,763	(39,692)	30,282	(11,818)	18,464
2008	92,518	(23,080)	5,844	(6,548)	(704)

### 5.9.2 Joint venture

#### Percivia LLC, United States

In August 2006, DSM Pharmaceutical Products Inc, and the Group established a joint venture, Percivia LLC (Percivia) to operate the PERCIVIA PER.C6 Development Center in Cambridge, MA, US. Each company holds 50% of the shares of the joint venture. The initial contribution of the Group amounted to \$ 500. The joint venture further develops the PER.C6 cell line and provides a unique solution for the production of pharmaceutical proteins to licensees utilizing the PER.C6 human cell line in the biotech industry. Percivia charges the costs incurred to the venturers. No additional contributions are planned.

Summary financial information of this joint venture, not adjusted for the percentage ownership held by the Group is as follows:

In thousand of Euro

Percivia LLC	As of December 31,		Year ended December 31,		
	Total assets	Total liabilities	Revenues	Expenses	Profit/ (loss) before tax
2009	3,888	(1,131)	9,154	(8,319)	835
2008	3,420	(1,440)	8,721	(7,972)	749

The tax charge for PERCIVIA PER.C6 Development Center is accounted for in the financial statements of the venturers. The tax charge recognized in the financial statements relating to the percentage owned by the Group amounts to € 142 in 2009 (2008: € 151).

### 5.10 Retirement benefit obligations

The Group provides employee benefit plans to most of its employees by means of various pension plans. These plans comply with local regulations and practices in the countries in which they operate and differ based on legal requirements, tax legislation, local customs and economic conditions in those countries. While the nature of the plans varies by country, in general, the benefits provided depend on remuneration and years of service. Most of these benefits are administrated by insurance companies or pension funds.

In 2009 the Group changed its policy in accounting for actuarial gains and losses of defined benefit pensions plans. Starting 2009, the Group recognizes actuarial gains and losses in the period in which they occur in other comprehensive income. Previously, the Group accounted for its actuarial gains and losses arising from experience-based adjustments and changes in actuarial assumptions in line with the 'corridor' method as prescribed in IAS 19.92.

The Group adjusted comparative amounts disclosed for each prior period presented as if the new accounting policy had always been applied. See note 1.5.1 'New adopted accounting policies in the financial year 2009' in the financial statements for further details on the change in accounting policy.

# Notes to the consolidated financial statements continued

In thousands of Euro

Year ended December 31,	2009	2008	2007
Statement of income			
Defined benefit plans	(73)	254	220
Defined contribution plans	2,241	2,410	2,436
<b>Total</b>	<b>2,168</b>	<b>2,664</b>	<b>2,656</b>

As of December 31,	2009	2008	2007
Statement of financial position			
Defined benefit plans			
Pension assets	2,923	8,612	7,397
Pension liability	(4,437)	(4,009)	(3,699)
Net pension asset – (liability)	(1,514)	4,603	3,698

The Group operates defined benefit plans in Switzerland, Korea and Sweden. The pension asset of € 2,923 (2008: € 8,612) relates to the Swiss pension fund while the pension liability of € 4,437 (2008: € 4,009) relates to the Swedish and the Korean pension funds.

In total, 95% of the plan assets (2008: 97%) and 90% of the defined benefit obligation (2008: 91%) relate to the Swiss pension fund. The Swiss mandatory pension fund is organized in a foundation. The regular retirement age is 65, with the possibility of early retirement from the age of 59 and postponement of retirement up to the age of 68. Contributions by employees vary per age category and range from 1.25% for employees between 18 and 24 to 8.75% of the insured income for employees between 60 and 68. Contributions by the employer also vary per age category and range from 1.75% for employees between 18 and 24 to a maximum contribution of 22.25% of the insured income for employees between 60 and 68. The retirement pension at the age of 65 amounts to 6.4% of the accrued retirement assets at retirement. The Swiss pension fund provides a minimum benefit to its participants, which is mandatory under Swiss law. In case of an underfunding of the pension fund the employer is obliged to make an additional contribution to the pension fund.

The assumptions used in the actuarial calculation can have a significant impact on the outcome. The weighted average of the principal assumptions used in determining the employee benefit obligations for the defined benefit plans of the Group are shown below:

Year ended December 31,	2009	2008	2007
Discount rate	3.42%	3.37%	3.40%
Expected return on plan assets	4.54%	4.53%	4.53%
Future salary increases	1.22%	1.19%	1.22%
Future pension increases	0.75%	0.71%	0.78%

Changes in the present value of the defined benefit obligation are as follows:

In thousands of Euro

Year ended December 31,	2009	2008	2007
<b>Defined benefit obligation, January 1,</b>	<b>85,485</b>	<b>74,506</b>	<b>72,679</b>
Past service cost – vested obligations	(1,563)	—	—
Interest cost	2,860	2,165	2,363
Current service cost	3,926	3,748	3,369
Benefits paid	(3,100)	(4,418)	(2,450)
Actuarial (gains)/ losses	1,088	3,038	934
Exchange differences	608	6,446	(2,389)
<b>Defined benefit obligation, December 31,</b>	<b>89,304</b>	<b>85,485</b>	<b>74,506</b>

Changes in the fair value of plan assets are as follows:

In thousands of Euro

Year ended December 31,	2009	2008	2007
<b>Fair value of plan assets, January 1</b>	<b>92,211</b>	<b>99,032</b>	<b>102,306</b>
Expected return on plan assets	4,132	4,606	4,528
Acquisition of subsidiaries	—	—	—
Contributions by employer	2,074	598	2,338
Contributions by participants	1,164	1,053	984
Benefits paid	(3,100)	(4,418)	(2,450)
Actuarial gains/ (losses)	2,265	(17,961)	(5,727)
Exchange differences	677	9,301	(2,947)
<b>Fair value of plan assets, December 31</b>	<b>99,423</b>	<b>92,211</b>	<b>99,032</b>

In 2010, the Group expects to contribute € 2,100 to its defined benefit pension plans. The actual return on plan assets for the year ended December 31, 2009 amounted to a gain of € 6,397 (2008: loss of € 13,355).

The costs for defined benefit plans are as follows:

In thousands of Euro

Year ended December 31,	2009	2008	2007
Current service cost	<b>3,926</b>	3,748	3,369
Interest cost	<b>2,860</b>	2,165	2,363
Expected return on plan assets	<b>(4,132)</b>	(4,606)	(4,528)
Past service cost	<b>(1,563)</b>	—	—
Employee contributions	<b>(1,164)</b>	(1,053)	(984)
	<b>(73)</b>	<b>254</b>	<b>220</b>

The amounts recognized in other comprehensive income are as follows:

In thousands of Euro

Year ended December 31,	2009	2008	2007
The effect of changes in the asset ceiling	<b>9,394</b>	(20,157)	(8,465)
Actuarial (gains) and losses	<b>(1,177)</b>	20,999	6,661
	<b>8,217</b>	<b>842</b>	<b>(1,804)</b>
As of December 31,	2009	2008	2007
<b>Cumulative actuarial (gains) and losses</b>	<b>6,757</b>	<b>(1,460)</b>	<b>(2,302)</b>

The amounts in the statement of financial position are determined as follows:

In thousands of Euro

	December 31, 2009	December 31, 2008	January 1, 2007
Defined benefit obligation	<b>(89,304)</b>	(85,485)	(72,679)
Fair value of plan assets	<b>99,423</b>	92,211	102,306
Funded status	<b>10,119</b>	6,726	29,627
Amount not recognized as asset due to asset ceiling	<b>(11,633)</b>	(2,123)	(30,493)
Net pension (liability)/ asset	<b>(1,514)</b>	4,603	(866)

The impact of the change in accounting policy on the net pension liability as at January 1, 2007 is an amount of € 248. The total net pension liability as at January 1, 2007 increased from € 618 to € 866.

In thousands of Euro

Year ended December 31,	2009	2008	2007	2006
Defined benefit obligation	<b>(89,304)</b>	(85,485)	(74,506)	(72,679)
Plan assets	<b>99,423</b>	92,211	99,032	102,306
Surplus	<b>10,119</b>	6,726	24,526	29,627
Experience adjustments on plan liabilities – (loss)/gain	<b>(0.4)%</b>	(3.0)%	(1.7)%	1.1%
<b>Experience adjustments on plan assets – (loss)/gain</b>	<b>2.2%</b>	<b>(10.0)%</b>	<b>(5.8)%</b>	<b>(0.2)%</b>

The major categories of plan assets as a percentage of the fair value of total plan assets are as follows:

	2009	2008
Bonds	<b>42.2%</b>	44.9%
Equity	<b>24.3%</b>	22.0%
Property	<b>25.1%</b>	28.4%
Other	<b>8.4%</b>	4.7%
	<b>100.0%</b>	<b>100.0%</b>

The overall expected rate of return on assets is determined based on the market prices expected to be applicable to the period over which the obligation is to be settled and the relative weight of the separate categories of plan assets.

# Notes to the consolidated financial statements continued

## 5.11 Other financial assets

In thousands of Euro

As of December 31,	2009	2008
Long-term restricted cash	13,023	12,896
Long-term deposits and guarantees	2,870	1,645
Other long-term receivables	325	379
	16,218	14,920

## 5.12 Cash and cash equivalents

In thousands of Euro

As of December 31,	2009	2008
Cash at banks and in hand	95,297	91,853
Call deposits	232,540	79,116
	327,837	170,969

Cash and cash equivalents are denominated in the following currencies (translated into Euros):

In thousands of Euro

As of December 31,	2008	2008
Euros (€)	256,711	111,909
Korean Won (KRW)	35,047	7,360
US Dollar (\$)	24,907	37,975
Swedish Crowns (SEK)	4,570	7,746
Canadian Dollars (CAD)	3,459	50
Pound Sterling (£)	1,610	5
Swiss Francs (CHF)	1,210	4,144
Other currencies	323	1,780
	327,837	170,969

## 5.13 Derivative financial instruments

The Group uses derivative financial instruments for the management of foreign currency risks.

In thousands of Euro

As of December 31,	2009 Fair value assets	2009 Fair value liabilities	2009 Total fair value	2008 Fair value assets	2008 Fair value liabilities	2008 Total fair value
Foreign exchange contracts	229	(294)	(65)	1,761	(194)	1,567
Cash flow hedge	57	—	57	—	(685)	(685)
Total derivative financial instruments	286	(294)	(8)	1,761	(879)	882



All derivative financial instruments mature within a year and are therefore presented as current assets or liabilities. The fair values of forward foreign exchange contracts are determined using forward foreign exchange rates as at December 31, 2009.

All foreign exchange contracts, which are not designated as a qualifying hedge instrument, mature within 2 months after December 31, 2009. The principal amount and fair value of foreign currency forwards that are not designated in a cash flow hedge are € 26,856 in 2009 (2008: € 38,907) and have a negative unrealized result of € 65 in 2009 (2008: positive unrealized result of € 1,567). The Group enters in these derivative transactions to mitigate its foreign currency transaction exposure.

### Cash flow hedging

The Group has designated certain qualifying derivative financial instruments as hedge instruments for cash flow hedge accounting to manage its currency risk resulting from specific contracts denominated in foreign currencies that differ from the functional currency of the Group company that engages in the contract. The principal amount and fair value of foreign currency forwards designated in a cash flow hedge are € 4,486 (2008: € 7,535) and an unrealized result of € 57 (2008: € 685) respectively.

Cash flow hedges of foreign currency risks relate to forecasted transactions. These are expected to occur between four and nine months after December 31, 2009. As at year-end 2009, the outstanding cash flow hedge was estimated to be 100% effective. No ineffectiveness was recognized in the statement of income arising from cash flow hedges (2008: Nil).

### 5.14 Trade accounts receivable

In thousands of Euro

As of December 31,	2009	2008
Trade receivables from third party customers	<b>86,910</b>	39,343
Trade receivables from associates and joint ventures	<b>121</b>	765
	<b>87,031</b>	<b>40,108</b>

At December 31, 2009, trade accounts receivables are shown net of an allowance for doubtful debts for an amount of € 1,924 (2008: € 2,289). The Group's normal credit period is 30 days, although in some jurisdictions, including Italy, Korea and Spain, a credit period of 60 days or even more is maintained in line with local customs. Receivables are denominated in several currencies and can be specified as follows:

In thousands of Euro

As of December 31,	2009	2008
Euros (€)	<b>32,003</b>	20,569
US Dollar (\$)	<b>34,434</b>	8,985
Swiss Francs (CHF)	<b>12,211</b>	5,058
Swedish Crowns (SEK)	<b>6,833</b>	2,810
Korean Won (KRW)	<b>417</b>	1,334
Other currencies	<b>1,133</b>	1,352
	<b>87,031</b>	<b>40,108</b>

# Notes to the consolidated financial statements continued

## Aging of past due, but not impaired

Included in the Group's trade accounts receivables balance are debtors with a carrying amount of € 16,010 (2008: € 11,678) which are past due at the reporting date for which the Group has no significant provision because there has not been a significant change in credit quality and the amounts are considered recoverable. The Group does not hold any collateral over these balances.

In thousands of Euro

As of December 31,	2009	2008
0-60 days	10,136	7,810
60-90 days	2,524	1,407
90-180 days	888	340
Over 180 days	2,462	2,121
	<b>16,010</b>	<b>11,678</b>

The Group's trade accounts receivables past due, but not impaired, are mainly due within the European region (€ 13,629). These are mainly due from customers in the Mediterranean region, which normally pay after the standard payment period and due from significant customers, whose trade accounts receivables have recently shifted into the overdue buckets.

## Allowance for doubtful debts

Movements in the allowance for doubtful debts are as follows:

In thousands of Euro

Year ended December 31,	2009	2008
Balance at beginning of the year	2,289	2,763
Impairment losses recognized on receivables	166	1,429
Amounts written off as uncollectible	(300)	(1,379)
Amounts recovered during the year	(51)	(8)
Impairment losses reversed	(190)	(281)
Foreign exchange	10	(235)
	<b>1,924</b>	<b>2,289</b>

## 5.15 Inventories

In thousands of Euro

As of December 31,	2009	2008
Raw materials and consumables	22,560	13,286
Work in progress	85,667	61,980
Finished products	10,193	16,581
	<b>118,420</b>	<b>91,847</b>

In order to be able to meet the demand from the market (e.g. in case of outbreak of a disease) the Group stocks certain inventories to a level such that they may not be utilized within one year. Provisions are recognized for obsolete inventory. The amount of write-down of inventories recognized as an expense is € 1,689 (2008: € 3,218).

The amount of inventories recognized as an expense in cost of product sales is € 173,391 (2008: € 128,632; 2007: € 113,250).

### 5.16 Other current assets

In thousands of Euro

As of December 31,	2009	2008
Accrued income	6,368	4,495
Prepaid expenses	4,415	3,612
Other short-term receivables	1,900	6,658
Director's loan	134	134
Income tax receivables	8,680	2,734
Deposits with a maturity over 3 months	100,000	—
	<b>121,497</b>	<b>17,633</b>

### 5.17 Issued share capital and reserves

The Company's authorized share capital amounts to 156,250,000 ordinary shares and 156,250,000 preference shares, each with a par value of € 0.24. As of December 31, 2009, there were 81,446,295 ordinary shares issued and outstanding (2008: 65,833,242). No preference shares are issued and outstanding as of December 31, 2009.

	Shares 000	Issued capital € 000	Share premium € 000	Total capital € 000
At December 31, 2007	65,349	15,685	735,578	751,263
Shares issued relating to share-based payments	484	115	3,115	3,230
Cost of share-based payment transactions	—	—	5,053	5,053
At December 31, 2008	65,833	15,800	743,746	759,546
Shares issued relating to share-based payments	986	237	8,969	9,206
Cost of share-based payment transactions	—	—	7,732	7,732
Shares issued in relation to private placement of JNJ	14,627	3,510	228,549	232,059
<b>At December 31, 2009</b>	<b>81,446</b>	<b>19,547</b>	<b>988,996</b>	<b>1,008,543</b>

The Dutch Civil Code restricts distribution of legal reserves and capital in an amount of € 28,077 (2008: € 19,054).

### Strategic collaboration affiliates of Johnson & Johnson (JNJ)

On September 28, 2009 Crucell signed a strategic agreement with affiliates of JNJ. On that date the Group entered into several agreements with affiliates of JNJ: an equity purchase agreement, a registration rights agreement, a shareholder agreement and two collaboration agreements.

Pursuant to the equity purchase agreement the Company issued 14,626,984 shares to JHC Nederland B.V., an affiliate of JNJ, at a price of € 20.63, totaling an amount of € 301,755. The number of shares issued represents 18% of the outstanding share capital of the Company after issuance. The equity purchase agreement contains customary representations and warranties.

## Notes to the consolidated financial statements continued

Under IFRS, the fair value of the equity investment corresponds with a total value of € 233,300. The fair value per share was equal to the price of a NYSE Euronext listed share of the Company at the date of issuance. Costs directly attributable to the issuance of shares amount to € 1,241 and are deducted from share premium, a component of equity. The premium over the fair value of € 68,455 has been allocated to the development programs that are part of the strategic collaboration with an affiliate of JNJ, as described below.

The Group and JNJ, through its subsidiary Ortho-McNeil-Janssen Pharmaceuticals, Inc., entered into a strategic collaboration for the development and commercialization of a universal monoclonal antibody product (flu-mAb) for the treatment and prevention of influenza. In addition, the strategic collaboration involves three innovative discovery programs focusing on the development and commercialization of a universal influenza vaccine as well as vaccines directed against three other infectious and non-infectious disease targets. Pursuant to the registration rights agreement, JHC Nederland B.V. was granted certain customary rights regarding the registration of the new shares issued to it under the US Securities Exchange Act 1934, as amended.

The following is a summary of certain important elements of the shareholder agreement.

**Standstill** For a certain period beginning September 28, 2009, JHC Nederland B.V. and its affiliates may not, without the Group's prior approval, purchase or acquire any shares or securities of the Company convertible into, or exercisable or exchangeable for, or otherwise giving the holder thereof any rights in respect of, shares or commence a public offer for the Company's shares, if, in either case, the consummation of such purchase or acquisition or public offer would result in JHC Nederland B.V. and its affiliates in the aggregate beneficially owning (assuming the exercise, exchange or conversion of all our securities held by them), directly or indirectly, more than 18% of the issued and outstanding shares of the Company. Customary exceptions apply to the standstill.

**Anti-Dilution** If, within nine months from the date of issuance, the Company experiences the consummation of a negotiated transaction for a change of control of the Company at a price per share below the issue price, JHC Nederland B.V. shall be entitled to receive a cash payment equal to the difference between the issue price and such lower price multiplied by the number of shares acquired upon consummation of such transaction (not to exceed the number of 14,626,984 new shares as acquired by JHC Nederland B.V. on the issue date). This amount must be paid to JHC Nederland B.V. within 5 business days after the consummation of the relevant transaction by the counterparty to the change of control transaction or where it concerns a public offer or sale of all or substantially all of our assets by the Company.

**Drag Along Right** If the Company receives a bona fide public offer from a third party and (i) the Management Board and Supervisory Board have endorsed, approved, recommended or otherwise supported such public offer, (ii) the holders of at least 70% of the issued and outstanding shares of the Company (including those held by JHC Nederland B.V. and/or its affiliates) have tendered their shares to the third party in connection with such public offer and (iii) JHC Nederland B.V. and/or any of its affiliates do not have a bona fide matching (x) counter public offer to the Company's shareholders or (y) other proposal involving the acquisition by a third party of more than 30% of the Company's shares or assets pending, JHC Nederland B.V. and its affiliates shall agree to tender and sell all their shares in such public offer. JHC Nederland B.V. shall in such event, if applicable, also have the right to receive payment of the amount as described under 'Anti-Dilution' in the preceding paragraph.

**Pre-Emptive Right** If the Company plans to issue any shares or any securities convertible into, or exercisable or exchangeable for, or otherwise giving the holder thereof any rights in respect of, shares, JHC Nederland B.V. has the right to purchase in such offer such number of shares to maintain its proportionate ownership interest in the Company on a fully diluted basis (disregarding equity based awards under the Employee stock ownership plan (ESOP)). JHC Nederland B.V. pre-emptive right shall expire and no longer be available

upon JHC Nederland B.V. (together with its affiliates) ceasing to beneficially own at least 12% of the Company's issued and outstanding shares of the Company.

**Approval Rights** the Company may not without the approval of JHC Nederland B.V.: (i) commence a tender offer or repurchase of shares if the consummation of such tender offer or repurchase would result in JHC Nederland B.V. holding more than 18% of the issued and outstanding shares, (ii) grant options or other equity awards in excess of the amounts authorized under the ESOP, or (iii) amend the Articles of Association in a manner that would create a new class of securities, or make the current rights of the General Meeting subject to proposals of the Management Board and/or Supervisory Board or subject to other limitations. JHC Nederland B.V. approval right shall expire and no longer be available upon JHC Nederland B.V. (together with its affiliates) ceasing to beneficially own at least 10% of the Company's issued and outstanding shares.

## 5.18 Share-based payment plans

### Stock-based compensation

#### Employee stock option plans

The Group maintains stock option plans whereby the Remuneration committee of the Supervisory Board may grant options to employees, directors and members of the Supervisory Board. The compensation expenses included in operating expenses for those plans were € 7,732, € 5,053 and € 6,524 in 2009, 2008 and 2007, respectively.

In December 2004, the Supervisory Board approved a new option plan (the '2005 Plan') providing for the grant of stock options to non-Management Committee members. Options granted under this stock option plan are exercisable once vested. Granted options vest straight line over a period of four years. Compensation costs are recognized in accordance with the accelerated method. The options expire five years after date of grant. Upon termination of employment, options must be exercised within 90 days. Options granted under the stock option plan are granted at exercise prices, which equal the fair value of the ordinary shares of the Company at the date of grant.

All options granted under previous stock option plans (the 'Prior Plans') are exercisable immediately upon grant. The options expire four to eight years from the date of grant, or earlier upon termination of employment with the Group. Upon termination of employment, options must be exercised within 90 days. No further grants are to be made under the Prior Plans.

The Group has a separate long-term incentive (LTI) stock option for its Management Committee members. Under the terms of the LTI plan, options are conditionally granted and vest at the end of a three-year performance period. The conditionally granted options include a market condition that is taken into account when estimating the fair value of the equity instruments granted. The number of LTI options that vest are based on the fulfillment of the LTI performance condition. On the vesting date, the Company's Total Shareholder Return ('TSR') performance is measured against the performance of the NASDAQ Biotechnology Index during the performance period. The positive difference in percentages, if any, between the Company's TSR compared to the performance of the NASDAQ Biotechnology Index, determines the number of LTI options that vest on the vesting date. Depending on the level of achievement of these market measures, at the end of three years, the number of shares vesting could be 0%-200% of the number of options originally granted.

The Group accounts for its employee stock options under the fair value method. The fair value of options is estimated at the date of grant using the Black-Scholes option-pricing model, with the following weighted average assumptions:

Year ended December 31,	2009	2008	2007
Risk-free interest rate	2.4%	4.3%	4.1%
Expected dividend yield	—	—	—
Expected volatility	50.9%	36.7%	33.3%
Expected life (years)	4.39	4.76	4.25

The weighted average fair value of options granted during the years ended December 31, 2009, 2008 and 2007 was € 6.68, € 4.03 and € 5.34, respectively.

## Notes to the consolidated financial statements continued

A summary of the stock option activity for the outstanding plans is as follows:

	Number of options	Weighted average exercise price
<b>Balance at January 1, 2007</b>	<b>3,685,440</b>	<b>10.36</b>
Granted	1,514,165	16.97
Exercised	(301,475)	6.45
Forfeited	(237,447)	19.15
<b>Balance at December 31, 2007</b>	<b>4,660,683</b>	<b>12.31</b>
Granted	2,639,640	11.59
Exercised	(420,270)	7.58
Forfeited	(592,175)	16.55
<b>Balance at December 31, 2008</b>	<b>6,287,878</b>	<b>11.92</b>
Granted	1,179,986	14.41
Exercised	(958,569)	9.57
Forfeited	(376,357)	14.77
<b>Balance at December 31, 2009</b>	<b>6,132,938</b>	<b>12.59</b>

Included in the options outstanding are also options to acquire ordinary shares held by certain former employees and consultants. These individuals have been permitted to continue vesting in these options for services rendered.

During 2009, a number of 134,306 conditionally granted LTI options were issued. These LTI options are included in the total number of options outstanding as of December 31, 2009.

The following table summarizes information about the company's stock options outstanding at December 31, 2009:

Exercise price	Outstanding options at December 31, 2009	Weighted average exercise price	Weighted average remaining contractual life (years)	Exercisable options	Weighted average exercise price-exercisable options
€ 2.35 – € 5.00	489,100	3.33	1.12	489,100	3.33
€ 5.00 – € 9.99	918,315	7.43	2.22	617,885	6.49
€ 10.00 – € 14.99	3,298,396	12.96	3.84	379,125	13.09
€ 15.00 – € 19.99	1,227,546	17.88	2.23	678,782	18.06
€ 20.00 – € 22.22	199,581	20.42	1.18	155,006	20.47
<b>Total</b>	<b>6,132,938</b>	<b>12.59</b>	<b>2.99</b>	<b>2,319,898</b>	<b>11.22</b>

### Stock option grants to non-employees

Crucell has a total number of 55,000 (2008: 67,604) stock options to various non-employees outstanding in connection with consulting agreements over the years. The exercise prices range from € 14.58 to € 18.22 per share and the stock options expire on dates ranging from May 2010 through August 2012.

The Company recorded compensation expense associated with these stock options of € 23, € 24, and € 11 for the years ended December 31, 2009, 2008 and 2007, respectively.

Stock option grants to non-employees are made pursuant to approved stock option plans and activity related thereto is included in the tables above with the employee grants of the approved plans.

### 5.19 Provisions, commitments and contingencies

In thousands of Euro

	Restructuring	Litigation	Employee Benefits	Other	Total
<b>At January 1, 2008</b>	<b>—</b>	<b>855</b>	<b>3,699</b>	<b>1,013</b>	<b>5,567</b>
Arising during the year	684	705	—	626	2,015
Utilised	(74)	(2)	—	(491)	(567)
Unused amounts reversed	—	—	—	(33)	(33)
Movement defined benefit liability	—	—	(207)	—	(207)
Exchange adjustment	—	90	517	75	682
<b>At December 31, 2008</b>	<b>610</b>	<b>1,648</b>	<b>4,009</b>	<b>1,190</b>	<b>7,457</b>
Current 2008	610	—	—	971	1,581
Non-current 2008	—	1,648	4,009	219	5,876
<b>At January 1, 2009</b>	<b>610</b>	<b>1,648</b>	<b>4,009</b>	<b>1,190</b>	<b>7,457</b>
Arising during the year	300	247	—	911	1,458
Utilised	(541)	(88)	—	(934)	(1,563)
Unused amounts reversed	(69)	—	—	(134)	(203)
Movement defined benefit liability	—	—	399	—	399
Exchange adjustment	—	4	29	11	44
<b>At December 31, 2009</b>	<b>300</b>	<b>1,811</b>	<b>4,437</b>	<b>1,044</b>	<b>7,592</b>
Current 2009	—	—	—	739	739
Non-current 2009	300	1,811	4,437	305	6,853

The impact of the change in accounting policy on provisions as at January 1, 2007 is an amount of € 248, which is due to an increase of the employee benefits. The total provision as at January 1, 2007 increased from € 8,006 to € 8,354.

#### Restructuring provisions

In May 2009, Management decided to move the formulation and filling activities relating to Dukoral and rCTB to our Madrid site. A restructuring provision of € 300 is recognized for redundancy packages offered to employees. In 2008, a restructuring program in our Italian subsidiary Berna Biotech Italia Srl. was executed. A total provision of € 684 was recognized of which € 610 was outstanding as per year-end 2008. An amount of € 541 was utilized in 2009. The remaining amount of € 69 was released.

#### Legal proceedings

The Group is subject to certain lawsuits and other legal proceedings. The current status of any pending proceedings has been reviewed with a legal counsel. Upon consideration of known relevant facts and circumstances, provisions are recognized for losses that are considered to be probable and that can be reasonably estimated at the year-end.

#### Deductibility of research and development costs

In Italy, Berna Biotech Italia Srl. was subject to a tax audit for fiscal years 2001 and 2002. For the year 2001, a settlement was reached with the Italian tax authorities in 2007. For the year 2002, no settlement has been reached. The tax authorities issued an assessment that deviates from the amount that was filed in the tax return. We have challenged this assessment



## Notes to the consolidated financial statements continued

in court. We made a provision for the costs of additional taxes, penalties and interest, as well as lawyers' fees, which we expect we would have to pay as a result. One of the items in dispute is the deductibility of the research and development costs we make in Italy. The Group won the initial court case with respect to the deductibility of the research and development costs. The Italian tax authorities appealed this decision.

In 2008, the Italian tax authorities also challenged the deductibility of research and development costs for the year 2003 and issued an assessment. We challenged this assessment in court. The Group won the initial court case with respect to the deductibility of the research and development costs. The Italian tax authorities appealed this decision. The Italian tax authorities may also challenge the deductibility of research and development costs for the years 2004 to 2008. As the Group considers it more likely than not that the research and development cost will be tax deductible, consequently no provision was recognized for the non-deductibility of research and development costs for the year 2003.

### **Complaint against government grant awarded**

In 2008, a competitor of Crucell filed a protest against the award of a US Government grant to Crucell for the development and manufacture of a vaccine against the Ebola and Marburg virus. The complaint was filed against the US Government but Crucell voluntarily joined the proceedings to defend the award. Following a dismissal of the protest by the US Government Accountability Office (GAO), the competitor filed an appeal with the United States Court of Appeals for the Federal Circuit. In the second quarter of 2009, this appeal by the competitor was also dismissed.

### **Employee benefits**

See note 5.10 'Retirement benefit obligations' for more information on employee benefits.

### **Other**

The other provisions mainly include provisions for product returns and asset retirement obligations. The provision for product returns amounts to € 589 and is established for expected product returns to be incurred within one year. The asset retirement obligations mainly related to our Swiss subsidiary and are expected to be settled after one year.

### **Contingencies**

#### **Contingent liability STAR technology**

The Group acquired STAR technology in 2004 through the purchase of ChromaGenics B.V., a privately held biotechnology company based in Amsterdam. In connection with the purchase, we also entered in a contingent payment agreement that could result in additional payments of up to € 7.0 million to former ChromaGenics shareholders upon receipt of revenues and royalties generated from the STAR technology. In connection with this agreement, we paid € 2.0 million in 2007 to former ChromaGenics shareholders. No payments were made in 2009 and 2008.

## 5.20 Short and long-term financial liabilities

This note provides information about the contractual terms of the Group's loans and borrowings. See note 3 'Financial risk management' for more information on the Group's exposure to financial market risks.

In thousands of Euro

As of December 31,	Total 2009	2010	2011	2012	2013	2014	More than 5 years	Total 2008
Mortgage loan	<b>16,094</b>	384	401	420	441	462	13,986	16,461
Equipment lease	<b>17,924</b>	3,099	3,426	6,158	1,786	3,455	—	20,526
Comprehensive credit limit Berna Biotech Korea Corp.	<b>14,990</b>	14,990	—	—	—	—	—	20,855
Mortgage loan Korea	<b>2,998</b>	—	—	—	—	2,998	—	—
Loan Berna Biotech Korea Corp.	<b>—</b>	—	—	—	—	—	—	2,909
Derivatives	<b>294</b>	294	—	—	—	—	—	879
	<b>52,300</b>	<b>18,767</b>	<b>3,827</b>	<b>6,578</b>	<b>2,227</b>	<b>6,915</b>	<b>13,986</b>	<b>61,630</b>

### Mortgage loan Netherlands

In December 2005, the Group entered into a Euro mortgage loan of up to € 17,091 and as of December 31, 2006 the Group had drawn the maximum amount. In 2006, interest was accrued to the loan and no payments of principal or interest were required. Beginning January 1, 2007, the loan is being repaid through monthly payments over 15 years. A balloon repayment of € 10,000 will be made at the end of the 15 years. The loan matures on December 31, 2021. The loan bears interest at 4.55% for the first five years. After this period the rates will be renegotiated. The land, building, part of the equipment and a compensating cash balance arrangement with a bank in the amount of € 10,000 secure the loan. The carrying amount of the underlying secured assets was at the year-end € 22,396 (2008: € 24,015 2007: € 26,946).

### Finance lease liabilities

Finance leases mainly relate to equipment for the new production facility in Leiden. The vast majority of the finance lease liabilities are denominated in Euro. All leases are on a fixed repayment basis and interest rates are fixed at the contract date. For further information see note 5.23 'Operating and finance leases'.

### Comprehensive credit limit Berna Biotech Korea Corp.

On June 12, 2008 Berna Biotech Korea Corp. entered into a comprehensive credit limit transaction agreement. Under the terms of the agreement Berna Biotech Korea Corp. may freely borrow and repay money for an amount of KRW 30 billion during the period ending on May 31, 2009. In December 2008, Berna Biotech Korea Corp. agreed on an additional facility for KRW 10 billion. The loan has a variable interest rate that is based on a Korean interest index plus a margin. As per year-end the interest percentage was 6.79% and an amount of KRW 37 billion (€ 20,855) was drawn under the agreement.

### Loan Berna Biotech Korea Corp.

Berna Biotech Korea Corp. had an unsecured Euro loan with an interest rate of 5.45% which was outstanding as at December 31, 2008. The original maturity date of the loan was August 1, 2010, but the loan was repaid in full on February 2, 2009.

### Mortgage loan Korea

On March 26, 2009, the Group's Korean subsidiary entered into a mortgage loan facility in an amount of KRW 50 billion (€ 27,704) with a Korean bank to partly finance the investments in the new Incheon facility. The loan has a duration of 60 months and has a variable interest rate that is based on a Korean interest index plus a mark-up. As at December 31, 2009, KRW 5 billion was drawn under the mortgage facility. The Group provided the third party bank with a guarantee amounting to KRW 50 billion plus interest and other costs.

# Notes to the consolidated financial statements continued

## 5.21 Other liabilities and deferred income – current and non-current

In thousands of Euro

As of December 31,	Current	Non-current	2009 Total	Current	Non-current	2008 Total
Deferred income	21,301	54,980	76,281	7,882	7,054	14,936
Accrued salary expenses and payroll taxes	12,231	—	12,231	9,817	—	9,817
Accrued expenses	11,731	—	11,731	8,540	—	8,540
Other liabilities	2,249	504	2,753	2,166	591	2,757
	47,512	55,484	102,996	28,405	7,645	36,050

### *Collaboration with an affiliate of JNJ*

On September 28, 2009, the Group entered into two collaboration agreements with Ortho-McNeil-Janssen Pharmaceuticals (an affiliate of JNJ) in conjunction with several other agreements (See 5.17 'Issued share capital and reserves'). The premium over the fair value of the shares paid by JNJ for the 18% equity investment amounted to € 68,455 and is classified as deferred income. The amount is amortized over the duration of the continuing performance obligations of the development programs.

## 5.22 Trade accounts payable

In thousands of Euro

As of December 31,	2009	2008
Trade accounts payable to third parties	<b>78,345</b>	58,182
Trade accounts payable to joint venture	<b>754</b>	1,023
	<b>79,099</b>	59,205

### 5.23 Operating and finance leases

#### Operating lease commitments

The Group leases certain research and corporate facilities, motor vehicles and items of machinery and equipment. No restrictions are placed upon the lessee by entering into these leases. Future minimum lease payments under operating leases as at December 31, 2009 and 2008 are as follows:

In thousands of Euro

As of December 31,	2009	2008
Within one year	<b>4,203</b>	3,830
After one year but not more than five years	<b>9,310</b>	10,073
More than five years	<b>9,533</b>	10,759
	<b>23,046</b>	24,662

Most operating leases are increased by a general price index on an annual basis.

#### Finance lease commitments

Certain of the Group's fixtures and equipment are subject to finance leases. These leases mainly relate to equipment for the new production facility in Leiden and the filling line in Spain. Interest rates are fixed at the contract date. All leases are on a fixed repayment basis and no arrangements have been entered into for contingent rental payments. The fair value of the Group's lease obligations approximates their carrying amount. The Group's obligations under finance leases are secured by the value of the underlying assets. The average term of finance leases entered into is 5.5 years.

Future minimum lease payments under finance leases as at December 31, 2009 and 2008 are as follows:

In thousands of Euro

As of December 31,	2009 Minimum payments	Present value of payments	2008 Minimum payments	Present value of payments
Within one year	<b>4,279</b>	3,099	4,134	2,777
After one year but not more than five years	<b>16,832</b>	14,825	17,284	14,293
More than five years	—	—	3,580	3,456
	<b>21,111</b>	<b>17,924</b>	<b>24,998</b>	<b>20,526</b>

# Notes to the consolidated financial statements continued

## 5.24 Financial instruments

### Financial assets

In thousands of Euro

As of December 31,	Financial assets at fair value through profit and loss	Designated cash flow hedge	Loans and receivables	Available-for-sale financial assets	2009 Total	Financial assets at fair value through profit and loss	Loans and receivables	Available-for-sale financial assets	2008 Total
Derivative financial instruments	229	57	—	—	286	1,761	—	—	1,761
Available-for-sale financial assets	—	—	—	10,441	10,441	—	—	4,922	4,922
Other financial assets	—	—	16,218	—	16,218	—	14,920	—	14,920
Cash and cash equivalents	—	—	327,837	—	327,837	—	170,969	—	170,969
Trade accounts receivables	—	—	87,031	—	87,031	—	40,108	—	40,108
Other current assets	—	—	110,713	—	110,713	—	9,526	—	9,526
	<b>229</b>	<b>57</b>	<b>541,799</b>	<b>10,441</b>	<b>552,526</b>	<b>1,761</b>	<b>235,523</b>	<b>4,922</b>	<b>242,206</b>

The carrying value of the financial assets approximates the fair value.

### Financial liabilities

In thousands of Euro

As of December 31,	Financial liabilities at fair value through profit and loss	Financial liabilities at amortized cost	2009 Total	Financial liabilities at fair value through profit and loss	Designated cash flow hedge	Financial liabilities at amortized cost	2008 Total
Derivative financial instruments	294	—	294	194	685	—	879
Financial liabilities	—	52,006	52,006	—	—	60,751	60,751
Other non-current liabilities	—	504	504	—	—	591	591
Accounts payable	—	79,099	79,099	—	—	59,205	59,205
Other current liabilities	—	26,211	26,211	—	—	20,523	20,523
	<b>294</b>	<b>157,820</b>	<b>158,114</b>	<b>194</b>	<b>685</b>	<b>141,070</b>	<b>141,949</b>

The fair values of the financial liabilities of the Group approximate the carrying amount of the Group's financial instruments.

The fair values of the loans have been calculated by discounting the face values with the interest rate of financial instruments with a similar risk profile and term. The fair values of forward foreign exchange contracts are determined using forward foreign exchange rates as at December 31, 2009.

### Maturity analysis contractual undiscounted cash flows

Future minimum payments for all contractual obligations for years subsequent to December 31, 2009 are as follows:

In thousands of Euro

As of December 31,	Total	Less than one year	1-3 years	3-5 years	More than 5 years
<b>Contractual obligations</b>					
Debt obligations <sup>1</sup>	42,767	16,627	2,638	5,639	17,863
Finance lease obligations <sup>2</sup>	21,111	4,266	11,159	5,686	—
Derivative financial instruments <sup>3</sup>	31,464	31,464	—	—	—
Accounts payable	79,099	79,099	—	—	—
Other current liabilities	26,715	26,211	504	—	—
<b>Recognised obligations</b>	<b>201,156</b>	<b>157,667</b>	<b>14,301</b>	<b>11,325</b>	<b>17,863</b>
<b>Commitments</b>					
Operating lease obligations <sup>4</sup>	23,046	4,203	5,787	3,523	9,533
Capital expenditure commitments <sup>5</sup>	15,755	15,755	—	—	—
<b>Total commitments</b>	<b>38,801</b>	<b>19,958</b>	<b>5,787</b>	<b>3,523</b>	<b>9,533</b>
<b>Total recognized obligations and commitments</b>	<b>239,957</b>	<b>177,625</b>	<b>20,088</b>	<b>14,848</b>	<b>27,396</b>

<sup>1</sup> The debt obligations exclude finance lease obligations and include an amount of interest of € 7,841.

<sup>2</sup> Finance lease obligations. Certain of the Group's fixtures and equipment are finance leases. The finance leases relate to equipment for the new production facility in Leiden, the Netherlands and to the filling line in Spain. Interest rates are fixed at the contract date. All leases are on a fixed repayment basis and no arrangements have been entered into for contingent rental payments. The interest included amounts to € 3,187.

<sup>3</sup> Derivative financial instruments are foreign exchange contracts. The principal amount and fair value of foreign currency forwards that are not designated in a cash flow hedge are € 26,856 in 2009 (2008: € 38,907) and have a negative unrealized result of € 65 in 2009 (2008: positive unrealized result of € 1,567). The principal amount and fair value of foreign currency forwards designated in a cash flow hedge are € 4,486 (2008: € 7,535) and an unrealized result of € 57 (2008: € 685), respectively.

<sup>4</sup> Operating lease obligations. The operating lease obligations include rental obligations. The Group concluded long-term rental agreements for premises in Sweden and the Netherlands. In addition, the Group leases certain motor vehicles and items of machinery and equipment.

<sup>5</sup> Capital expenditure commitments. The contractual commitments for purchases of property, plant and equipment as per December 31, 2009 amount to approximately € 15,755 (2008: € 20,380; € 4,696). These commitments mainly relate to our new production facility in Incheon, Free Economic Zone, Korea.

# Notes to the consolidated financial statements continued

## 5.25 Fair value estimation

Effective 1 January 2009, the Group adopted the amendment to IFRS 7 for financial instruments that are measured in the statement of financial position at fair value, this requires disclosure of fair value measurements by level of the following fair value measurement hierarchy:

- Quoted prices (unadjusted) in active markets for identical assets or liabilities (level 1).
- Inputs other than quoted prices included within level 1 that are observable for the asset or liability, either directly (that is, as prices) or indirectly (that is, derived from prices) (level 2).
- Inputs for the asset or liability that are not based on observable market data (that is, unobservable inputs) (level 3).

In thousands of Euro

As of December 31,	2009 Level 1	Level 2	Total	2008 Level 1	Level 2	Total
<b>Assets</b>						
Financial assets at fair value through profit or loss						
Derivative financial instruments	—	57	57	—	1,761	1,761
Available-for-sale financial assets	10,136	305	10,441	4,922	—	4,922
<b>Liabilities</b>						
Derivative financial instruments	—	(65)	(65)	—	(879)	(879)
<b>Total</b>	<b>10,136</b>	<b>297</b>	<b>10,433</b>	<b>4,922</b>	<b>882</b>	<b>5,804</b>

The Group did not have any assets at liabilities measured at fair value using significant unobservable inputs (Level 3) as of December 31, 2009 and 2008.

The fair value of financial instruments traded in active markets is based on quoted market prices at the year-end. A market is regarded active if quoted prices are readily and regularly available from an exchange, dealer, broker, industry group, pricing service, or regulatory agency, and those prices represent actual and regularly occurring market transactions on an arm's length basis. The quoted market price used for financial assets held by the group is the current bid price. These instruments are included in level 1. Instruments included in level 1 comprise primarily equity investments classified as trading securities or available-for-sale.

The fair value of financial instruments that are not traded in an active market (for example, over-the-counter derivatives) is determined by using valuation techniques. These valuation techniques maximise the use of observable market data where it is available and rely as little as possible on entity specific estimates. If all significant inputs required to fair value an instrument are observable, the instrument is included in level 2.

If one or more of the significant inputs is not based on observable market data, the instrument is included in level 3.

The Group did not reclassify any financial assets out of the fair value through profit and loss category or out of the available-for-sale category.



## 5.26 Guarantees

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The Group has a guarantee facility for an amount of € 10.0 million with a third-party bank.

In 2008, as part of the overall working capital management efforts, the Group agreed with Novartis to extend payment terms on the supply of Quinvaxem antigens. We have provided Novartis with collateral on our Swiss premises for an amount up to € 30,254. These payment terms still apply in 2009.

In addition to the guarantees given on assets, as described in note 5.6 'Property, plant and equipment' and note 5.20 'Short and long-term financial liabilities', the guarantees issued by the Group amount to € 4,414, which include a letter of credit issued by the Group for an amount of \$ 1.6 million, which will expire on April 14, 2013, for the benefit of the Percivia Development Center.

## 5.27 Net cash flows from/ (used in) operating activities

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In 2009, the Group's cash flow from operating activities was € 76,866, compared to a negative operating cash flow of € 254 in 2008. These cash flows consist of non-cash adjustments and changes in working capital relating to operating activities.

On September 28, 2009 Crucell signed a strategic agreement with JNJ. As part of this agreement the Company allocated an amount of € 68,455 to the development programs, which is presented as deferred income. The non-current part of € 51,341 is included in 'Receipt from (payments of) deferred income and provisions' and the current part of € 17,114 is included in the 'Changes in net working capital'.

## 5.28 Net cash flows from/ (used in) investing activities

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In 2009, the Group's cash flow used in investing activities amounted to € 154,387, compared to € 8,907 in 2008.

Investments were made in property, plant and equipment for an amount of € 51,035 (2008: € 15,787). These investments mainly related to our new Korean production facility and investments in our facilities in Bern, Switzerland that will improve current production processes and allow in-house production of materials currently sourced from third parties. In addition, investments were made in intangible assets in an amount of € 5,925.

An amount of € 100,000 was invested in deposits with a maturity over 3 months.

## 5.29 Net cash flows from/ (used in) financing activities

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In 2009, the total cash flow from financing activities amounted to € 231,512 in 2009, compared to € 16,626 in 2008.

The Company issued 14,626,984 shares to JHC Nederland B.V. an affiliate of JNJ. The fair value of the shares issued, after deducting directly attributable transaction costs, amounted to € 232,059. See note 5.17 'Issued share capital and reserves' for more information on the shares issued. Total cash proceeds resulting from share based payment transactions, mainly the exercise of options by employees, amounted to € 9,206 in 2009.

An amount of € 2,884 was drawn under a mortgage loan facility by the Group's Korean subsidiary in connection with the new production facility.

The Group's Korean subsidiary repaid an unsecured Euro-denominated in an amount of € 2,909 and partially repaid a KRW denominated flexible loan in amount of for € 6,757. The Group also repaid finance lease liabilities in the aggregate amount of € 2,984.

# Notes to the consolidated financial statements continued

## 5.30 Related parties

### Related party transactions

The Group has related party transactions and balances with joint venture partners, associates and directors and executive officers. All transactions with related parties were carried out under normal market conditions (arm's length principle). There are no related party transactions outside the normal course of business.

### Terms and conditions of transactions with related parties

The sales to and purchases from related parties are made at normal market prices. Outstanding balances at the year-end are unsecured, interest free and settlement occurs in cash. There have been no guarantees provided by the Group or received in respect of any related party receivables or payables. For the year ended December 31, 2009, the Group has not made any provision for doubtful debts relating to amounts owed by related parties (2008: nil). This assessment is undertaken each financial year through examining the financial position of the related party.

Transactions between the Company and its subsidiaries, which are related parties, have been eliminated on consolidation and are not disclosed in this note.

The following table provides the total value of transactions which have been entered into with related parties, excluding Management and Supervisory Board members, for the relevant financial year.

In thousands of Euro

	Revenue/(expenses) for the year ended December 31,		
Related party <sup>1</sup>	2009	2008	2007
Associates	2,825	3,392	2,858
Joint Venture	(4,170)	(4,081)	(4,247)

<sup>1</sup> Prior to 2009, transactions with Avv. Falaguerra, an Italian firm that provides taxation services to the Group's Italian subsidiary, were disclosed, as Mr. Falaguerra was the chairman of the Italian subsidiary. Mr. Falaguerra resigned in 2009 as chairman. Transactions with Mr. Falaguerra were limited in value and have not been disclosed any more.

As of December 31, 2009 trade accounts receivable in an amount of € 121 (2008: 4,495) were receivable from the Group's associate. As of December 31, 2009 trade accounts payable in an amount of € 754 (2008: 1,023) were payable to the Group's joint venture.

### Preferred foundation

On October 25, 2000, the Company established a foundation called Stichting Preferente Aandelen Crucell, also referred to as the Preferred Foundation. The Preferred Foundation's object is to safeguard the interests of Crucell, its business and parties connected therewith by blocking any influences that may threaten these interests, which interests may include the continuity, independence or identity of Crucell, its business and parties connected therewith. The Preferred Foundation can safeguard these interests through acquiring and managing the preference shares and by exercising the rights attaching to these shares, in particular, the voting rights.

The agreement between the Company and the Preferred Foundation grants an option to the Preferred Foundation to acquire preference shares up to 100% of the number of our outstanding shares as necessary to match the total number of statutory votes on all of the ordinary shares outstanding at the time of an acquisition. The Preferred Foundation must pay at least 25% of the nominal value of the preference shares it acquires from the Company. If the Company has previously acquired any preference shares, they may be cancelled.

A board of governors of up to five persons directs the Preferred Foundation. Mr. J.P. Oosterveld, in his capacity as chairman of our Supervisory Board, and Mr. P. Bouw, Mr. M.W. den Boogert, Mr. S. van Wijnbergen and Mr. G.P. Krans, have been appointed to the board of governors. A majority of these members may not be members or former members of the Management or Supervisory Board of the Company, or an employee of any of our advisers, any of our banks or us. The board of governors appoints these independent members. The Supervisory Board appoints the non-independent members after consultation with the Management Board.

In 2009, the Group funded the Preferred Foundation in an amount of € 100 (2008: nil, 2007: € 438).

As a result of the arrangements regarding the exercise of the options and restrictions to the use of the underlying shares by the Preferred Foundation, the Company is of the opinion that the option has an insignificant value.

#### **Remuneration report for Management Board and Supervisory Board**

The 'Remuneration report for Management Board and Supervisory Board' as included in the Corporate Governance section of the Management Report contains required disclosures on key management personnel compensation, as meant in IAS 24. These disclosures are deemed to be part of the financial statements.

# Company financial statements

## 6 Statement of financial position (After appropriation of result)

In thousands of Euro

As of December 31,	Notes	December 31, 2009	December 31, 2008 As adjusted	January 1, 2007 As adjusted
<b>Assets</b>				
Non-current assets				
Investments in subsidiaries	9.1	340,294	267,375	283,320
Other long-term receivables	9.2	34,648	49,272	141,089
Goodwill		37,529	37,239	35,456
		412,471	353,886	459,865
Current assets				
Short-term receivables		474	1,015	1,218
Cash and cash equivalents		262,449	79,295	38,094
Short term receivables related parties		108,227	18,614	—
		371,150	98,924	39,312
<b>Total assets</b>		<b>783,621</b>	452,810	499,177
<b>Liabilities and shareholders' equity</b>				
Shareholders' equity				
Issued capital		19,547	15,800	15,553
Share premium		988,996	743,746	726,869
Translation reserve (legal reserve)		(19,586)	(32,852)	(7,933)
Hedge reserve (legal reserve)		57	(685)	—
Available-for-sale reserve (legal reserve)		8,473	3,254	10,670
Actuarial gains and losses		(5,217)	1,214	383
Accumulated deficit		(254,005)	(277,943)	(247,859)
	9.3	738,265	452,534	497,683
Non-current liabilities				
Provision for financial assets		15,490	—	1,341
Liabilities to related parties		155	149	132
		15,645	149	1,473
Current liabilities				
Accrued compensation and related benefits		29,551	122	21
Liability to related parties		160	5	—
		29,711	127	21
<b>Total liabilities and shareholders' equity</b>		<b>783,621</b>	452,810	499,177

## 7 Statement of income

In thousands of Euro

Year ended December 31,	2009	2008 As adjusted	2007 As adjusted
Result from subsidiaries	18,647	3,683	(48,368)
Other income	5,291	10,567	4,034
<b>Profit/ (loss) for the year</b>	<b>23,938</b>	<b>14,250</b>	<b>(44,334)</b>

# Notes to the Company financial statements

## 8 General

The description of the Group's activities and the Group structure as included in the notes to the consolidated financial statements also apply to the Company financial statements (see note 1.1).

In accordance with article 2:362 section 8 of Book 2 Title 9 of the Dutch Civil Code, the accounting policies used in the preparation of the Company financial statements, except for investments, are the same as those used in the preparation of the consolidated financial statements. Investments in subsidiaries are stated at net asset value as the Company effectively exercises significant influence over the operational and financial activities of these investments. The net asset value is determined on the basis of the IFRS accounting principles applied by the Group in its consolidated financial statements.

In accordance with article 402, Book 2 Title 9 of the Dutch Civil Code, the Company statement of income is presented in abbreviated form.

## 9 Notes to the Company financial statements

### 9.1 Investments in subsidiaries

Investments in subsidiary companies are stated at net asset value as the Company effectively exercises significant influence over the operational and financial activities of these investments.

In thousands of Euro

Year ended December 31,	2009	2008	2007
<b>Book value as of January 1,</b>	<b>267,375</b>	<b>272,054</b>	<b>283,523</b>
Change in accounting policy	—	—	(203)
Share in result of subsidiaries	18,647	3,683	(48,368)
Effect of movements in exchange rates	12,976	(6,684)	(20,018)
Dividends received	—	(43,069)	(80,907)
Acquisition shares subsidiaries	—	—	80,907
Transfer to/ (from) provisions	15,490	—	(1,341)
Offset of receivables	26,961	47,062	59,375
Other comprehensive income items	(1,155)	(5,671)	(914)
<b>Book value at December 31,</b>	<b>340,294</b>	<b>267,375</b>	<b>272,054</b>

Other comprehensive income items include actuarial losses and gains on pensions, unrealized results on available-for-sale financial assets and changes in the cash flow hedge reserves of the Company's subsidiaries.

On June 12, 2008 Crucell Switzerland AG distributed a dividend equivalent to € 43,069 to the Company.

Beginning 2007, Crucell owned 7.3% of the shares of Berna Rhein B.V. The remaining 92.7% of the shares were owned by Crucell's subsidiary Crucell Switzerland AG. On November 3, 2007 Crucell acquired the remaining 92.7% shares for € 80,907. Crucell Switzerland AG subsequently distributed a dividend equivalent to € 80,907 to the Company.

# Notes to the Company

## financial statements continued

### 9.2 Other long-term receivables

In thousands of Euro

As of December 31,	December 31, 2009	December 31, 2008	January 1, 2007
Long-term receivables on related parties	21,625	36,376	126,693
Other long-term receivables	13,023	12,896	14,396
	34,648	49,272	141,089

### 9.3 Shareholders' equity

Reference is made to the consolidated statement of changes in equity and to note 5.17 'Issued share capital and reserves' of the notes to the consolidated financial statements as of, and for the year ended December 31, 2009.

### 9.4 Taxes

The Company constitutes a fiscal unity with the Dutch wholly owned subsidiaries Crucell Holland B.V., U-BiSys B.V. and ChromaGenics B.V. and is for that reason jointly and severally liable for the tax liabilities of the whole fiscal unity. As of the financial year 2008, Berna Rhein B.V. was included in that fiscal unity.

### 9.5 Employee information

The Company had no employees in 2009 and 2008.

### 9.6 Auditor's fees

	Year ended December 31, 2009			Year ended December 31, 2008		
	Deloitte Accountants B.V.	Network Deloitte Accountants B.V.	Total	Deloitte Accountants B.V.	Network Deloitte Accountants B.V.	Total
Audit fees	510	315	825	481	359	840
Audit related fees	149	—	149	75	—	75
Tax fees for services provided related to consultation on tax matters	—	—	—	—	—	—
<b>Total fees</b>	<b>659</b>	<b>315</b>	<b>974</b>	<b>556</b>	<b>359</b>	<b>915</b>

### 9.7 Joint and several liability

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In accordance with Section 403 of Book 2 Title 9 of the Netherlands Civil Code, the Company has assumed joint and several liability for all legal transactions carried out by the following subsidiaries:

Crucell Holland B.V., Leiden  
U-BiSys B.V., Utrecht  
ChromaGenics B.V., Amsterdam

### Signing of the financial statements

The financial statements were approved by the Management Board and Supervisory Board and authorized for issue on April 6, 2010.

#### Management Board

R.H.P. Brus  
L. Kruimer  
C. de Jong  
J. Goudsmit

#### Supervisory Board

J.P. Oosterveld  
A. Hoevenaars  
S.P. Lance  
P.M. Satow  
C.E. Wilhelmsson  
S. Davis  
F. Waller



# Other information

## Appropriation of result

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Annual dividends may only be paid out of profits as shown in the adopted annual financial statements. We may not make distributions if the distribution would reduce our shareholders' equity below certain reserves required by Dutch law or our articles of association. The profits must first be used to set up and maintain reserves required by Dutch law and must then be set off against certain financial losses. The preference shares will be paid their dividends first, which will be a certain percentage of their nominal value. With Supervisory Board approval, our Management Board then decides whether and how much of the remaining profit will be reserved. Any profits remaining shall be paid as a dividend on the ordinary shares. If the retained earnings are negative or are to be used to form a statutory reserve no dividend will be paid out. The result for the year 2009 was added to the accumulated deficit.

## Preference shares

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On October 25, 2000, the Company established a foundation called Stichting Preferente Aandelen Crucell, also referred to as the Preferred Foundation. The Preferred Foundation's object is to safeguard the interests of Crucell, its business and parties connected therewith by blocking any influences that may threaten these interests, which interests may include the continuity, independence or identity of Crucell, its business and parties connected therewith. The Preferred Foundation can safeguard the interests through acquiring and managing the preference shares and by exercising the rights attaching to these shares, in particular, the voting rights.

The Preferred Foundation has an option to acquire preference shares up to 100% of the number of our outstanding shares, necessary to match the total number of statutory votes on all of the ordinary shares outstanding at the time of an acquisition. The Preferred Foundation must pay at least 25% of the nominal value of the preference shares it acquires from us. If we acquire any preference shares, they may be cancelled.

A board of governors of up to five persons directs the Preferred Foundation. Mr. J.P. Oosterveld, in his capacity as chairman of our Supervisory Board, and Mr. P. Bouw, Mr. M.W. den Boogert, Mr. S. van Wijnbergen and Mr. G.P. Krans, have been appointed to the board of governors. A majority of these members may not be members or former members of our Management or Supervisory Board, or an employee of any of our advisers, any of our banks or us. The board of governors appoints these independent members. Our Supervisory Board appoints the non-independent members after consultation with our Management Board.

# Auditor's report

**To the Supervisory Board and Shareholders of Crucell N.V.,  
Leiden, The Netherlands**

## Report on the financial statements

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We have audited the accompanying financial statements 2009 as set out on pages 163 to 221 of Crucell N.V., Leiden. The financial statements consist of the consolidated financial statements and the company financial statements. The consolidated financial statements comprise the consolidated statement of financial position as at December 31, 2009, the consolidated statement of income, consolidated statement of comprehensive income, consolidated statement of changes in equity and consolidated statement of cash flow for the year then ended, and notes, comprising a summary of significant accounting policies and other explanatory notes. The company financial statements comprise the company statement of financial position as at December 31, 2009, the company statement of income for the year then ended and the explanatory notes.

## Management's responsibility

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Management is responsible for the preparation and fair presentation of the financial statements in accordance with International Financial Reporting Standards as adopted by the European Union and with Part 9 of Book 2 of the Netherlands Civil Code, and for the preparation of the management report in accordance with Part 9 of Book 2 of the Netherlands Civil Code. This responsibility includes: designing, implementing and maintaining internal control relevant to the preparation and fair presentation of the financial statements that are free from material misstatement, whether due to fraud or error; selecting and applying appropriate accounting policies; and making accounting estimates that are reasonable in the circumstances.

## Auditor's responsibility

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Our responsibility is to express an opinion on the financial statements based on our audit. We conducted our audit in accordance with Dutch law. This law requires that we comply with ethical requirements and plan and perform the audit to obtain reasonable assurance whether the financial statements are free from material misstatement.

An audit involves performing procedures to obtain audit evidence about the amounts and disclosures in the financial

statements. The procedures selected depend on the auditor's judgment, including the assessment of the risks of material misstatement of the financial statements, whether due to fraud or error. In making those risk assessments, the auditor considers internal control relevant to the entity's preparation and fair presentation of the financial statements in order to design audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the entity's internal control. An audit also includes evaluating the appropriateness of accounting policies used and the reasonableness of accounting estimates made by management, as well as evaluating the overall presentation of the financial statements.

We believe that the audit evidence we have obtained is sufficient and appropriate to provide a basis for our audit opinion.

## Opinion with respect to the consolidated financial statements

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In our opinion, the consolidated financial statements give a true and fair view of the financial position of Crucell N.V. as at December 31, 2009, and of its result and its cash flow for the year then ended in accordance with International Financial Reporting Standards as adopted by the European Union and with Part 9 of Book 2 of the Netherlands Civil Code.

## Opinion with respect to the company financial statements

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In our opinion, the company financial statements give a true and fair view of the financial position of Crucell N.V. as at December 31, 2009 and of its result for the year then ended in accordance with Part 9 of Book 2 of the Netherlands Civil Code.

## Report on other legal and regulatory requirements

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Pursuant to the legal requirement under 2:393 sub 5 part f of the Netherlands Civil Code, we report, to the extent of our competence, that the management report is consistent with the financial statements as required by 2:391 sub 4 of the Netherlands Civil Code.

Signed by:

**Deloitte Accountants B.V.**

P.J.M.A van de Goor

Amsterdam, the Netherlands

April 6, 2010

# Information for shareholders and investors

## Investor relations approach

Crucell maintains an active and transparent approach to relations with shareholders and investors. We inform the financial markets regularly about the Company's strategy and developments. Quarterly results releases, presentations and press releases on important business developments are disseminated on a regular basis and reinforced with briefings by phone and in person. Since August 2007, we have strengthened our Investor Relations activities with the addition of two dedicated Investor Relations Officers whose mission it is to ensure the investor community understands clearly the Company's prospects and performance. This reflects our ambition to widen our investor base as well as to deepen existing investors' understanding of Crucell.

Activities in 2009 for shareholders and investors comprised:

- A full presentation of quarterly results to financial journalists and analysts at each quarter, consisting of an online slide show and audio commentary, question and answer sessions and archiving for subsequent retrieval;
- Various additional telephone conference calls with management for analysts and investors;
- Regular road show meetings with potential and existing shareholders and sell-side analysts who cover the Company;
- Timely updates in the Investor Relations section of the website [www.crucell.com](http://www.crucell.com);
- Periodic website updates of more comprehensive financial Company data, including filings with the United States Securities and Exchange Commission; and
- Online publication of relevant scientific company presentations.

## Crucell shares

Crucell's ordinary shares are listed on:

- NYSE Euronext Amsterdam N.V. (symbol: CRXL) since 2000;
- NASDAQ in the US (symbol: CRXL) in the form of ADS's since 2000;
- SWX Swiss Exchange in Zurich (symbol: CRXL) since 2005;

The Company's primary listing is Amsterdam where trading turnover reached € 1.95 billion in 2009; Crucell's shares are included in the AMX mid-cap index (since 2005);

## Share data

Year ended December 31,	2009	2008
Earnings per share	<b>0.34</b>	0.22
Shares outstanding (million) at year-end	<b>81.4</b>	65.8
Dividend	—	—
Highest price	<b>17.61</b>	14.10
Lowest price	<b>10.78</b>	7.40
Price at December 31,	<b>13.90</b>	10.89
Average daily trading volume on Euronext Amsterdam (X 1,000)	<b>500</b>	465

## Shareholders with holdings of Crucell shares exceeding 5%

Percentage of beneficial ownership is based on an aggregate of 81,661,920 ordinary shares outstanding at March 29, 2010 except as otherwise noted:

Beneficial Owner	Ordinary Shares Beneficially Owned <sup>1</sup>	
	Number of Ordinary Shares	Holding (%)
JHC Nederland B.V.	14,626,984	17.91 <sup>2</sup>
A. van Herk B.V.	7,689,270	9.42 <sup>3</sup>
Ordinary shares held by our Management Board members	442,079	0.54
Ordinary shares held by our Supervisory Board members	142,210	0.17

<sup>1</sup> Under Rule 13d 3 of the Exchange Act, more than one person may be deemed to beneficially own certain ordinary shares (if, for example, persons share the power to vote or the power to dispose of the ordinary shares). In addition, a person is deemed to beneficially own ordinary shares if the person has the right to acquire the ordinary shares (for example, upon exercise of an option) within 60 days of the date as of which the information is provided. As a result, the percentage of outstanding ordinary shares of any person as shown in this table does not necessarily reflect the person's actual ownership or voting power with respect to the number of ordinary shares actually outstanding. In addition, filings with the Netherlands Authority for the Financial Markets (Autoriteit Financiële Markten or AFM) with respect to shareholdings in public companies do not specify the number of shares held by the filing party.

<sup>2</sup> Percentage holding is derived from a filing made by Johnson & Johnson with the Netherlands AFM.

<sup>3</sup> Percentage holding is derived from a filing made by A. van Herk B.V. with the Netherlands AFM.

As of March 29, 2010, there were 12,645,840 ADSs, each representing one ordinary share, all of which were held of record by five registered holders in the US (including The Depository Trust Company). The number of ADSs at March 29, 2010 represent 15.5% of our ordinary shares that were issued and outstanding on that date.

To the best of our knowledge, we are not directly or indirectly owned or controlled by any other corporation, foreign government or other person or entity.

### Share information

Crucell shares are included in the NYSE Euronext Amsterdam Dutch mid-cap index (AMX), and in the NASDAQ Composite Index. They are also included in the FTSE NASDAQ Small Cap index since 2005 and in the NYSE Euronext NEXT Biotech Index as of April 2008.

As of December 31,	2009	2008
Market Capitalization (€ million)	<b>1,131.5</b>	716.6
Market Capitalization (\$ million)	<b>1,630.0</b>	1,000.2
Closing share price (€)	<b>13.90</b>	10.89
Closing share price (\$)	<b>20.02</b>	15.20
Shares outstanding (million)	<b>81.4</b>	65.8

### Shareholder information

At December 31, 2009, institutional investors held approximately 51% of the outstanding shares in Crucell, private investors held 48% of shares and holdings of affiliates were approximately 1%.

Geographical spreads of shareholders in approximate percentages on December 31, 2009, compared to the previous year are as follows:

	2009	2008
The Netherlands	<b>60%<sup>1</sup></b>	68%
United States	<b>30%</b>	22%
Germany	<b>2%</b>	4%
United Kingdom	<b>1%</b>	3%
Scandinavia	<b>2%</b>	2%
Other	<b>5%</b>	1%
Total	<b>100%</b>	<b>100%</b>

<sup>1</sup> Including 18% shareholding by JHC Nederland B.V. ultimate parent company Johnson & Johnson is U.S. based.

### Outlook for 2010

We confirm the outlook as provided to the market on February 9, 2010:

- continued strong operating cash flow to accelerate product development;
- R&D spending to increase by over one-third;
- maintaining a healthy operating profit; and
- revenues and other operating income broadly in line with 2009<sup>1</sup>.

<sup>1</sup>In guidance currencies = EUR/USD rate of 1.41

### General information

#### Auditors

Deloitte Accountants B.V.

#### Legal Counsel

Allen & Overy LLP

Cleary Gottlieb Steen & Hamilton LLP

#### Tax Advisers

Ernst & Young

#### ADS Depository

Bank of New York Mellon

#### Investor Relations

Oya Yavuz, Vice President of Corporate Communications & Investor Relations

Frauke Groenevelt, Manager Investor Relations

Tel: +31 71 5197064

Email: ir@crucell.com

# Information for shareholders and investors continued

## Our ordinary shares and ADSs

Our ordinary shares are traded in the US solely in the form of ADSs, each ADS representing one ordinary share. Each ADS is evidenced by an American Depositary Receipt issued by The Bank of New York Mellon acting as depositary in respect thereof.

The following table sets forth the range of high and low closing prices, in US dollars, for our ADSs on the NASDAQ National Market for the periods indicated.

	ADSs	
	High	Low
<b>Annual information for the past five years</b>		
2005	29.95	12.30
2006	28.82	17.27
2007	28.96	16.08
2008	19.88	9.60
2009	25.38	15.65
<b>Quarterly information for the past two years</b>		
<b>2008</b>		
First Quarter	19.39	13.15
Second Quarter	19.88	15.47
Third Quarter	18.18	13.27
Fourth Quarter	15.86	9.60
<b>2009</b>		
First Quarter	23.29	15.65
Second Quarter	24.29	18.44
Third Quarter	25.38	21.45
Fourth Quarter	22.01	19.57
<b>2010</b>		
First Quarter	21.44	18.97
<b>Monthly information for the most recent six months</b>		
October 2009	22.01	19.57
November 2009	21.95	19.95
December 2009	21.89	19.92
January 2010	20.87	19.33
February 2010	20.22	18.97
March 2010 (until March 29)	21.44	19.29

Our ordinary shares trade on Eurolist by NYSE Euronext Amsterdam N.V. through the book-entry facilities of NEGICEF, Euroclear and Clearstream Luxembourg. For the ordinary shares the International Securities Identification Number (ISIN) code is NL0000358562, the Amsterdam Security Number is 35856 and the Common Code is 11907164.

The following table sets forth the range of high and low closing prices, in Euro, for our ordinary shares in the Netherlands for the periods indicated.

	Ordinary shares	
	High	Low
<b>Annual information for the past five years</b>		
2005	24.77	9.50
2006	23.49	14.04
2007	22.27	10.96
2008	13.26	7.77
2009	17.42	11.33
<b>Quarterly information for the past two years</b>		
<b>2008</b>		
First Quarter	13.26	8.55
Second Quarter	12.85	9.86
Third Quarter	12.10	9.15
Fourth Quarter	11.35	7.77
<b>2009</b>		
First Quarter	17.15	11.33
Second Quarter	17.20	14.31
Third Quarter	17.42	14.87
Fourth Quarter	15.38	13.48
<b>2010</b>		
First Quarter	15.62	13.77
<b>Monthly information for the most recent six months</b>		
October 2009	15.38	13.51
November 2009	14.65	13.48
December 2009	14.60	13.85
January 2010	14.49	13.77
February 2010	14.48	13.93
March 2010 (until March 29)	15.62	14.23

**Exchange rate information**

The following table sets forth, for the previous six months, the high and low Noon Buying Rates expressed in Euro per USD 1.00.

	High €	Low €
October 2009	0.69	0.67
November 2009	0.68	0.66
December 2009	0.70	0.66
January 2010	0.72	0.69
February 2010	0.74	0.72
March 2010 (until March 26)	0.75	0.73

On March 26, 2010 the Noon Buying Rate was \$ 1.00 = € 0.75. These rates may differ from the actual rates used in the preparation of our financial statements and other financial information appearing in this Annual Report.

**American Depositary shares**

The Bank of New York Mellon serves as the depositary (the 'Depositary') for Crucell's American Depositary Shares ('ADS') program. The Bank of New York Mellon has its principal executive office at One Wall Street, New York, New York 10286, the US. Pursuant to the deposit agreement between Crucell, the Depositary and owners and holders of ADS (the 'Deposit Agreement'), ADS holders may be required to pay various fees to the Depositary, and the Depositary may refuse to provide any service for which a fee is assessed until the applicable fee has been paid. In particular, the Depositary, under the terms of the Deposit Agreement, shall charge a fee of \$ 5.00 or less per 100 ADSs (or portion thereof) for (i) the issuance, execution and delivery of ADSs or (ii) the withdrawal of shares underlying the ADSs. In addition, ADS holders may be required under the Deposit Agreement to pay the Depositary (i) any tax, duty, governmental charge or fee or stock transfer or registration fee arising in connection with the foregoing transactions or otherwise, (ii) any expense resulting from the conversion of a foreign currency into US dollars and (iii) the expense of certain communications made, at the request of the ADS holder, by cable, telex or facsimile. The Depositary may (i) withhold dividends or other distributions or sell any or all of the shares underlying the ADSs in order to satisfy any tax or governmental charge and (ii) deduct from any cash distribution any tax payable thereon or the cost of any currency conversion.

**Fees Incurred in past annual period**

From January 1, 2009 to March 29, 2010, the Company received from the depositary \$ 196,580.42 (February 20, 2009)

and \$ 50,000.00 (September 19, 2009) for standard out-of-pocket maintenance costs for the ADSs (consisting of the expenses of postage and envelopes for mailing annual and interim financial reports, printing and distributing dividend checks, electronic filing of U.S. Federal tax information, mailing required tax forms, stationery, postage, facsimile, and telephone calls), any applicable performance indicators relating to the ADS facility, underwriting fees and legal fees.

**Fees to be paid in the future**

The Bank of New York Mellon, as depositary, has agreed to reimburse the Company for expenses they incur that are related to establishment and maintenance expenses of the ADS program. The depositary has agreed to reimburse the Company for its continuing annual stock exchange listing fees. The depositary has also agreed to pay the standard out-of-pocket maintenance costs for the ADSs, which consist of the expenses of postage and envelopes for mailing annual and interim financial reports, printing and distributing dividend checks, electronic filing of U.S. Federal tax information, mailing required tax forms, stationery, postage, facsimile, and telephone calls. It has also agreed to reimburse the Company annually for certain investor relationship programs or special investor relations promotional activities. In certain instances, the depositary has agreed to provide additional payments to the Company based on any applicable performance indicators relating to the ADS facility. There are limits on the amount of expenses for which the depositary will reimburse the Company, but the amount of reimbursement available to the Company is not necessarily tied to the amount of fees the depositary collects from investors.

The depositary collects its fees for delivery and surrender of ADSs directly from investors depositing shares or surrendering ADSs for the purpose of withdrawal or from intermediaries acting for them. The depositary collects fees for making distributions to investors by deducting those fees from the amounts distributed or by selling a portion of distributable property to pay the fees. The depositary may collect its annual fee for depositary services by deduction from cash distributions or by directly billing investors or by charging the book-entry system accounts of participants acting for them. The depositary may generally refuse to provide fee-attracting services until its fees for those services are paid.

# Information for shareholders and investors continued

## Taxation

The following is a summary of the material Dutch and US tax consequences of an investment in ordinary shares or ADSs. This summary does not discuss every aspect of taxation that may be relevant to a particular investor who is subject to special treatment under any applicable law, and is not intended to be applicable in all respects to all categories of investors. This summary also assumes that our business will be conducted in the manner outlined in this document. Changes in our organizational structure or the manner in which we conduct our business may invalidate this summary. The laws upon which this summary is based are subject to change, perhaps with retroactive effect. A change to these laws may invalidate the contents of this summary, which will not be updated to reflect changes in the laws. Prospective investors should consult their professional tax advisers regarding their particular personal tax consequences of acquiring, owning and disposing of our ordinary shares or ADSs.

## Certain Dutch tax consequences for holders of ordinary shares or ADSs

This summary describes the principal tax consequences that will generally apply in the case of an investment in the ordinary shares or ADSs under Dutch tax laws in force and in effect as of the date hereof, and is subject to changes in Dutch law, including changes that could have retroactive effect. Not every potential tax consequence of such investment under the laws of the Netherlands will be addressed.

## Dutch taxation of resident shareholders

The summary of certain Dutch taxes set out in this section 'Dutch Taxation of Resident Shareholders' is only intended for the following investors:

- Individuals who are resident or deemed to be resident or who have opted to be resident in the Netherlands for purposes of Dutch taxation and who invest in the ordinary shares or ADSs, excluding individuals who invest in the ordinary shares or ADSs that form part of a substantial

interest (as described below) or deemed substantial interest in us and excluding individuals who are our employees or who are deemed to be our employees or employees of any entity related to us (the 'Dutch Individuals'); and

- Corporate entities (including associations which are taxable as corporate entities) that are resident or deemed to be resident in the Netherlands for purposes of Dutch taxation and who invest in the ordinary shares or ADSs; excluding:
- Corporate entities that are not subject to Dutch corporate income tax;
- Pension funds (pensioenfondsen) and other entities that are wholly or partly exempt from Dutch corporate income tax;
- Corporate entities that hold ordinary shares or ADSs that qualify for application of the participation exemption (as laid down in the Dutch Corporate Income Tax Act 1969); and
- Investment institutions (beleggingsinstellingen) and tax exempt investment institutions (vrijgestelde beleggingsinstellingen) as defined in the Dutch Corporate Income Tax Act 1969; (the 'Dutch Corporate Entities').

Generally, a holder of ordinary shares or ADSs will not have a substantial interest if he, his spouse, certain other relatives (including foster children) or certain persons sharing his household, do not hold, alone or together, whether directly or indirectly, the ownership of, or certain other rights over, ordinary shares representing 5% or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of shares), or rights to acquire ordinary shares, whether or not already issued, that represent at any time 5% or more of our total issued and outstanding capital (or the issued and outstanding capital of any class of shares) or the ownership of certain profit participating certificates that relate to 5% or more of our annual profit and/or to 5% or more of our liquidation proceeds.

## Individual and corporate income tax

For Dutch Individuals not engaged or deemed to be engaged in an enterprise and Dutch individuals for whom the benefits



derived from the ordinary shares or ADSs are not treated as 'result from other activities', the following applies:

The taxable benefit from a Dutch Individual's 'savings and investments' (sparen en beleggen) is set annually at 4% of the average of the so-called 'yield basis' (rendements grondslag) at the beginning and at the end of a year, insofar as the average exceeds the 'exempt net asset amount' (heffingvrij vermogen). Such taxable benefit is reduced by such portion of the personal allowance as has not been taken into account in respect of certain other types of income. This benefit is taxed at the rate of 30%. For Dutch Individuals who invest in the ordinary shares or ADSs, the ordinary shares or ADSs will form part of the yield basis. The ordinary shares or ADSs will be taken into account in the yield basis at their fair market value. The actual benefits from the ordinary shares or ADSs do not influence the taxable benefit, even if they exceed, or are lower than, 4% of the yield basis.

For Dutch Individuals engaged or deemed to be engaged in an enterprise, Dutch Individuals for whom the benefits derived from the ordinary shares or ADSs are treated as result from other activities, and Dutch Corporate Entities, the following applies:

Any benefits derived or deemed to be derived from the ordinary shares or ADSs (including any capital gains realized on the disposal thereof) that are attributable to an enterprise carried on in the Netherlands by a Dutch Individual or to an enterprise effectively managed in the Netherlands in which he has an interest, are generally subject to income tax charged at progressive rates. The same applies to a Dutch Individual for whom the benefits derived from the ordinary shares or ADSs are treated as result from other activities. Any benefits derived or deemed to be derived from the ordinary shares or ADSs (including any capital gains realized on the disposal thereof) that are held by a Dutch Corporate Entity are generally subject to corporate income tax.

### Withholding tax

Dividends we distribute are generally subject to a withholding tax imposed by the Netherlands at a rate of 15%. The concept 'dividends we distribute' used in this section includes, but is not limited to:

- Distributions in cash or in kind, deemed and constructive distributions and repayments of paid-in capital not

recognized for Dutch dividend withholding tax purposes;

- Liquidation proceeds, proceeds of redemption of the ordinary shares or ADSs or, as a rule, consideration for the repurchase of the ordinary shares or ADSs by us in excess of the average paid-in capital recognized for Dutch dividend withholding tax purposes;
- The par value of the ordinary shares or ADSs issued to a holder of the ordinary shares or ADSs or an increase of the par value of the ordinary shares or ADSs, as the case may be, to the extent that it does not appear that a contribution, recognized for Dutch dividend withholding tax purposes, has been made or will be made; and
- Partial repayment of paid-in capital, recognized for Dutch dividend withholding tax purposes, if and to the extent that there are net profits (zuivere winst), unless:
  - The general meeting of our shareholders has resolved in advance to make such repayment;
  - The par value of the ordinary shares or ADSs concerned has been reduced by an equal amount by way of an amendment of the articles of association; and
- Dutch Individuals and Dutch Corporate Entities generally can credit the dividend withholding tax against their income tax or corporate income tax liability and will be entitled to a refund of dividend withholding tax insofar as such tax, together with any other creditable domestic and/or foreign taxes, exceeds their aggregate income tax or corporate income tax liability. To avoid 'dividend stripping', a condition to be able to credit dividend withholding tax is that the recipient of proceeds from the ordinary shares or ADSs qualifies as the beneficial owner thereof. A recipient of proceeds from the ordinary shares or ADSs is not considered to be the beneficial owner thereof if the amount of dividend, following a set of transactions, is ultimately wholly or partly received by another person, if this other person also retains, directly or indirectly, an interest in the ordinary shares or ADSs and the recipient is entitled to a (partial) refund or exemption to which the other person is not entitled.

### Gift and inheritance taxes

A gift tax liability will arise in the Netherlands with respect to an acquisition of the ordinary shares or ADSs by way of a gift made by a Dutch individual or a Dutch corporate entity. An inheritance tax liability will arise in the Netherlands with respect to an acquisition or deemed acquisition of the ordinary shares or ADSs on the death of a Dutch individual.

For purposes of Dutch gift and inheritance taxes, an individual of Dutch nationality will be deemed to be resident

## Information for shareholders and investors continued

in the Netherlands if he has been resident in the Netherlands at any time during the ten years preceding the date of the gift or his death. For purposes of the Dutch gift tax, an individual not holding Dutch nationality will be deemed to be resident in the Netherlands if he has been resident in the Netherlands at any time during the 12 months preceding the date of the gift.

### Taxation of US investors

The following is a summary of the material US federal income tax considerations regarding the purchase, ownership and disposition of ordinary shares or ADSs to you if you are an “eligible US holder” (as defined below) but it does not purport to be a comprehensive description of all of the tax considerations that may be relevant to you or your situation, including tax considerations that arise from rules of general application to all taxpayers or to certain classes of investors or that are generally assumed to be known by you. In particular, the summary does not address considerations that may be applicable to you if you will not hold ordinary shares or ADSs as capital assets, if you are not an eligible US holder, or if you are a taxpayer subject to special tax rules, such as a bank, tax-exempt entity, insurance company, a regulated investment company, a pension fund, a real estate investment trust, a dealer in securities or currencies, a person that holds ordinary shares or ADSs as part of an integrated investment (including a ‘straddle’) comprised of ordinary shares or ADSs and one or more other positions, a person that holds ordinary shares or ADSs as a position in a synthetic security, hedging transaction or conversion transaction, a person liable for the alternative minimum tax and a person who owns or is deemed to own 10% or more of any class of our stock. The summary is based on laws, treaties and regulatory interpretations in effect on the date of this document, all of which are subject to change.

*You should consult your own advisers regarding the tax consequences of an investment in the ordinary shares or ADSs in light of your particular circumstances, including the US tax considerations discussed below and the effect of any state, local or other national laws.*

You are an eligible US holder if you are a resident of the US for purposes of the tax treaty between the Netherlands and the US (the ‘tax treaty’) and are fully eligible for benefits under the tax treaty. You generally will be entitled to the benefits of the tax treaty if you are:

- The beneficial owner of ordinary shares or ADSs (and of the dividends paid with respect to such ordinary shares or ADSs);
- A “US person” (i.e., an individual resident of the US, a US corporation, or a partnership, estate or trust to the extent your income is subject to taxation in the US as the income of a resident, in your hands or in the hands of your partners or beneficiaries);
- Not resident in the Netherlands for Dutch tax purposes; and
- Not subject to an anti-treaty shopping rule.

You generally will not be eligible for the benefits of the tax treaty, and therefore will not be an eligible US holder, if you hold ordinary shares or ADSs in connection with the conduct of business through a permanent establishment, or the performance of services through a fixed base in the Netherlands, or you are not resident in the US for US tax purposes.

If a partnership (or other entity treated as a partnership for US tax purposes) holds ordinary shares or ADSs, the tax treatment of a partner generally will depend upon the status of the partner and the activities of the partnership. If you are a partner in a partnership (or other entity treated as a partnership for US tax purposes) that holds ordinary shares or ADSs, you should consult your own tax adviser regarding the specific tax consequences of owning and disposing of ordinary shares or ADSs.

Based on our audited financial statements and relevant market data, we believe that we were not treated as a ‘passive foreign investment company’ or ‘PFIC’ for US federal income tax purposes with respect to the year 2009. In addition, based on our current expectations regarding the value and nature of our assets, the sources and nature of our

income, and relevant market data, we do not anticipate becoming a PFIC in the year 2010 or thereafter. We believe, however, that we were or may have been a PFIC for US federal income tax purposes with respect to the years before 2005. See 'Passive Foreign Investment Company Rules,' below. *US holders that held our ordinary shares or ADSs at any time before 2005 should consult their own tax advisers regarding the possible application of the PFIC rules to their ordinary shares or ADSs.*

For US federal income tax purposes beneficial owners of ADSs will be treated as the owners of the underlying ordinary shares represented by those ADSs.

### **Taxation of dividends**

The gross amount of distributions paid by us (including amounts withheld in respect of Dutch withholding tax) generally will be subject to US federal income taxation as foreign source ordinary dividend income to the extent paid or deemed paid out of our current or accumulated earnings and profits (as determined under US federal income tax principles), and will not be eligible for the dividends received deduction allowed to corporations. Distributions in excess of current and accumulated earnings and profits will be treated as a non-taxable return of capital to the extent of your basis in our ordinary shares or ADSs and thereafter as capital gain. However, we do not maintain calculations of earnings and profits and you should therefore assume that any distribution we make with respect to our ordinary shares and ADSs will constitute ordinary dividend income.

Subject to certain exceptions for positions that are hedged or held for less than 60 days, an individual US holder generally will be subject to US taxation at a maximum rate of 15% in respect of dividends received before January 1, 2011, unless we were in the year prior to the year in which the dividend was paid, or are, in the year in which the dividend is paid, a PFIC. As described above, we believe that we were not a PFIC for US tax purposes with respect to the year 2009, and also do not anticipate becoming a PFIC with respect to the year 2010.

Dividends paid in Euro will be included in income in a US dollar amount calculated by reference to the exchange rate in effect on the date of receipt by you (or by the depository in the case of ADSs). If such dividends are converted into US dollar on the date of receipt, you generally should not be required to recognize foreign currency gain or loss in respect of the dividend income. If you receive a refund of Dutch

withholding tax under the tax treaty between the Netherlands and the US, you may be required to recognize foreign currency gain or loss to the extent the amount of the tax treaty refund (in dollars) received by you differs from the US dollar equivalent of the refund amount on the date the dividends were received.

You may claim the benefit of the reduced withholding rate of 15% that is available under the tax treaty between the Netherlands and the US by submitting a duly completed Form IB 92 (USA) (available at [www.belastingdienst.nl](http://www.belastingdienst.nl)) that has been certified by a financial institution (typically the entity that holds the ordinary shares or ADSs as custodian for the holder). If we receive the required documentation prior to the relevant dividend payment date, we may apply the reduced withholding rate at source. If you fail to satisfy these requirements prior to the payment of a dividend, you may claim a refund of the excess of the amount withheld over the tax treaty rate by filing Form IB 92 (USA) together with a supplemental statement with the Dutch tax authorities. Pension funds and tax-exempt organizations qualifying for a complete exemption from tax are not entitled to claim tax treaty benefits at source, and instead must file claims for refund by filing Form IB 95 (USA) (also available at [www.belastingdienst.nl](http://www.belastingdienst.nl)).

Subject to applicable limitations and to the special considerations discussed below, Dutch withholding tax at the 15% tax treaty rate will be treated as a foreign income tax that is eligible for credit against your US federal income tax liability or, at your election, may be deducted in computing taxable income. Foreign tax credits will not be allowed for withholding taxes imposed in respect of certain short-term or hedged positions and may not be allowed in respect of arrangements in which your expected economic profit, after non-US taxes, is insubstantial. You should consult your own advisers concerning the implications of these rules in light of your particular circumstances.

### **Taxation of capital gains**

Subject to the discussion below under 'Passive Foreign Investment Company Rules', gain or loss realized by you on the sale or other disposition of ordinary shares or ADSs will be capital gain or loss in an amount equal to the difference between your basis in the ordinary shares or ADSs and the dollar-value of the amount realized on the disposition. (If the amount realized is denominated in a foreign currency, such amount shall be determined at the spot rate on the date of disposition, or, at the spot rate on the settlement date if the

## Information for shareholders and investors continued

shares or ADSs are traded on an established securities market and you are a cash basis eligible US holder or an accrual basis eligible US holder that so elects). The gain or loss will be long-term gain or loss if the ordinary shares or ADSs were held for more than one year. Long-term capital gain recognized by an individual US holder before January 1, 2011 generally is subject to taxation at a maximum rate of 15%.

### Passive foreign investment company rules

Unfavourable US tax rules (the 'PFIC rules') apply to companies that are considered passive foreign investment companies ('PFICs'). We will be classified as a PFIC in a particular taxable year if either (a) 75% or more of our gross income is treated as passive income for purposes of the PFIC rules; or (b) the average percentage of the value of our assets that produce or are held for the production of passive income is at least 50%.

As explained above, we believe that we were not a PFIC for US tax purposes with respect to the year 2009, and also do not anticipate becoming a PFIC with respect to the year 2010 and thereafter. We believe, however, that we were or may have been a PFIC for US federal income tax purposes with respect to the years before 2005.

If we were a PFIC in the past, US holders that held our ordinary shares or ADSs at any time during the years when we were a PFIC and did not make certain US tax elections (a "mark-to-market election" or a "QEF election") will be subject to adverse tax treatment. For instance, such holders will be subject to a special tax at ordinary income tax rates on certain dividends that we pay and on gains realized on the sale of ordinary shares or ADSs ("excess distributions") in all subsequent years, even though we ceased to qualify as a PFIC. The amount of this tax will be increased by an interest charge to compensate for tax deferral, calculated as if the excess distributions had been earned ratably over the period the US holder held its ordinary shares or ADSs. It may be possible, in certain circumstances, for a holder to avoid the application of the PFIC rules by making a "deemed sale" election for its taxable year that includes the last day of our last taxable year during which we qualified as a PFIC.

*The PFIC rules are extremely complex, and you should consult your own tax advisers regarding the possible application of the PFIC rules to your ordinary shares or ADSs and the desirability and availability of a "deemed sale election."*

### US backup withholding tax and information reporting

Payments in respect of the ordinary shares or ADSs that are made in the US or by a US-related financial intermediary will be subject to information reporting and may be subject to backup withholding unless you: (a) are a corporation or other exempt recipient; or (b) provide an IRS Form W-9 or an acceptable substitute form, certifying your taxpayer identification number and that no loss of exemption from backup withholding has occurred.

If you are not a US citizen or a "US person" (as defined in the introduction to this discussion), you generally are not subject to these rules, but may be required to provide certification of non-US status in order to establish that you are exempt.

### Documents on display

We are subject to the informational requirements of the Securities Exchange Act of 1934, as amended, and in accordance therewith file information with the US Securities and Exchange Commission ("SEC"). You may read and copy this information at the following location:

#### Public Reference Room

**100 F Street, N.E.  
Washington, D.C. 20549  
USA**

Please call the SEC at 1 800 SEC 0330 for further information on the public reference room. Copies of these materials can also be obtained by mail at prescribed rates from the Public Reference Section of the Securities and Exchange Commission, 100 F Street, N.E., Washington, D.C. 20549. Our ADSs are quoted on the NASDAQ National Market, and consequently, the periodic reports and other information filed by us with the Commission can be inspected at the

offices of the NASDAQ National Market, 1735 K Street, N.W., Washington, D.C. 20006. The primary market for our ordinary shares is NYSE Euronext Amsterdam. We make our filings with the SEC by electronic means. Any filings we make electronically are available to the public over the internet at the Commission's website at [www.sec.gov](http://www.sec.gov) and at our website at [www.cruce.com](http://www.cruce.com).

### Exchange Controls

There are currently no Dutch laws, decrees or regulations that restrict the export or import of capital, including, but not limited to, foreign exchange controls, or that affect the remittance of dividends or other payments to non-Dutch residents or to US holders of our securities except as otherwise set forth in 'Taxation' in this section.

### Significant changes

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Other than as disclosed in this Annual Report, no significant change has occurred since December 31, 2009, the date of our most recent audited financial statements.

### Limitation of liability and indemnification matters

Pursuant to Dutch law, each member of our Supervisory and Management Boards is responsible to us for the proper performance of his or her assigned duties. They are also responsible for taking measures to prevent the consequences of any improper performance of duties by another member of our Supervisory Board or our Management Board. Our articles of association provide that our Management Board members and our Supervisory Board members are discharged from liability for their actions as board members if our General Meeting of Shareholders adopts a resolution to that effect. This discharge extends only to actions or omissions disclosed in or apparent from the adopted annual accounts or otherwise communicated to our General Meeting of Shareholders.

This discharge of liability may be limited by mandatory provisions of Dutch law, such as in the case of bankruptcy. Under Dutch law, our Supervisory Board members and members of our Management Board generally cannot be held personally liable for decisions made exercising their reasonable business judgment.

Our articles of association provide that we shall generally indemnify any person who is or was a member of our Supervisory Board or our Management Board or one of our employees, officers or agents, and who suffers any loss as

a result of any action in connection with their service to us, provided they acted in good faith in carrying out their duties.

This indemnification generally will not be available if the person seeking indemnification acted with gross negligence or wilful misconduct in the performance of their duties to us. A court in which an action is brought may, however, determine that indemnification is appropriate nonetheless.

# Appendix overview licensees and partners

See below an overview of the Group's most significant licensees and partners:

## Vaccines

Partner/licensee	Starting date	Technology	Disease target	Development stage
Aeras Global TB Vaccine Foundation	Mar. 2004	PER.C6 and AdVac	Tuberculosis	Phase 2
Bestewil Holding B.V.	Jan. 2006	Co-micelles	Influenza	Pre-clinical
Harvard School of Medicine	Dec. 2003	AdVac + Ad5HVR48	HIV	Pre-clinical
International AIDS Vaccine Initiative (IAVI)	Sep. 2004	AdVac	HIV	Phase 1
Kimron Veterinary Institute	Jul. 2003	PER.C6	West Nile virus – Veterinary vaccine (avian)	Marketed in Israel
Merck & Co., Inc.	Nov. 1998	PER.C6	Undisclosed vaccines	Phase 1
Merck & Co., Inc.	Sep. 2007	PER.C6 and AdVac	2 Infectious disease areas	Pre-clinical
National Institutes of Health (NIH)	Mar. 2002	PER.C6 and AdVac	Ebola, lassa and Marburg	Phase 1
National Institutes of Health (NIH)	Mar. 2004	PER.C6 and AdVac	Malaria	Phase 1
Okairos Srl.	Oct. 2005	PER.C6	Hepatitis C	Phase 1
Sanofi pasteur	Dec. 2003	PER.C6	Influenza	Phase 2
TapImmune Inc.	Nov. 2009	PER.C6	Undisclosed vaccine	Pre-clinical
Transgene SA	Dec. 2007	PER.C6	Undisclosed vaccine	Pre-clinical
Vaxin, Inc.	Sep. 2004	PER.C6	Alzheimers disease and veterinary	Pre-clinical

## Proteins

Partner/licensee	Starting date	Technology	Disease target	Development stage
Abraxis Bioscience, LLC.	Oct. 2008	PER.C6	Protein production	Pre-clinical
Affitech AS	Nov. 2008	PER.C6	Undisclosed Antibodies	Pre-clinical
Bioceros B.V.	May 2008	STAR	Portfolio antibodies	Pre-clinical
Biotechnol SA	Jan. 2007	PER.C6	Portfolio antibodies	Pre-clinical
Cangene Corp.	Oct. 2008	PER.C6	Undisclosed Antibodies	Pre-clinical
Centocor, Inc.	Dec. 2008	STAR	Monoclonal antibodies	Pre-clinical
CSL Ltd.	Dec. 2008	PER.C6	Undisclosed protein	Pre-clinical
Daiichi Sankyo Co., Ltd.	Nov. 2007	PER.C6	Portfolio antibodies	Pre-clinical
Ferring International Center SA	May 2005	PER.C6	Women's healthcare	Pre-clinical
Ferring International Center SA	Dec. 2005	PER.C6	Women's healthcare	Pre-clinical
Gedeon Richter PLC	Nov. 2008	PER.C6	Undisclosed biopharmaceutical	Pre-clinical
GlaxoSmithKline Biologicals SA	Dec. 2008	PER.C6	Recombinant protein	Pre-clinical
Invitrogen Corp.	Sep. 2007	STAR	Monoclonal antibodies	Pre-clinical
IQ Corporation B.V.	Oct. 2005	PER.C6	Anti-anthrax antibody	Pre-clinical
LFB Biotechnologies	Jul. 2007	PER.C6	Undisclosed antibodies	Pre-clinical
JSC Masterclone	Jul 2007	PER.C6	Undisclosed antibodies	Pre-clinical
Merus B.V.	Jun. 2004	PER.C6	Portfolio oligoclonics	Pre-clinical
MorphoSys AG	Apr. 2008	PER.C6	Oncology	Pre-clinical
MorphoSys AG	Aug. 2006	PER.C6	Inflammatory diseases	Phase 2
MorphoSys AG	Aug. 2004	PER.C6	Portfolio antibodies	Pre-clinical
Novartis Vaccines and Diagnostics	Jun. 2004	PER.C6	Portfolio antibodies	Pre-clinical

Oy Medix Biochema AB	Dec. 2009	PER.C6	Recombinant antibodies	Pre-clinical
Patrys Ltd.	Aug. 2009	PER.C6	Undisclosed protein	Pre-clinical
Patrys Ltd.	Jul. 2009	PER.C6	Monoclonal antibodies	Pre-clinical
Pharmathene, Inc.	Dec. 2009	PER.C6	Undisclosed protein	Pre-clinical
ProFibrix B.V.	Dec. 2008	PER.C6	Recombinant fibrinogen	Pre-clinical
ProFibrix B.V.	Dec. 2008	PER.C6	Recombinant thrombin	Pre-clinical
Synthon B.V.	Nov. 2008	PER.C6	Biosimilar protein	Pre-clinical
Taiwanese Development Center for Biotechnology	Mar. 2007	PER.C6	Undisclosed proteins	Pre-clinical
TalecrisBiotherapeutics Inc.	Dec. 2008	PER.C6	Undisclosed proteins	Pre-clinical
TalecrisBiotherapeutics Inc.	Sep. 2008	PER.C6	Undisclosed protein	Pre-clinical
Thrombolytic Science Int., Inc.	Oct. 2009	PER.C6	Undisclosed protein	Pre-clinical
Toyobo Gene Analysis Co. Ltd.	Apr. 2008	STAR	Portfolio antibodies	Pre-clinical

### Gene therapy

Partner/licensee	Starting date	Technology	Disease target	Development stage
Ark Therapeutics Ltd.	Jan. 2006	PER.C6	Portfolio	Phase 3
Cancer Research UK Centre	Jan. 2010	PER.C6	Oncology	Pre-clinical
Elm Biotech Pty Ltd.	Dec. 2008	PER.C6	Adenovirus-vectored product	Pre-clinical
TAPImmune Inc.	Aug. 2003	PER.C6	Portfolio	Pre-clinical
Merck & Co., Inc.	Nov. 1998	PER.C6	Portfolio	Pre-clinical
Momotaro-Gene Inc.	Aug. 2009	PER.C6	Prostate cancer	Phase 1
NeoTropix, Inc.	Mar. 2004	PER.C6	Oncology	Pre-clinical
Transgene SA	Apr. 2001	PER.C6	Portfolio	Phase 2
Vascular Biogenics Ltd.	Mar. 2005	PER.C6	Portfolio	Phase 2

### Alliances with contract managers for production

Partner/licensee	Starting date	Technology	Area
Avid Bioservices, Inc.	Jul. 2008	PER.C6	Protein production services
Bioceros	Jan. 2009	PER.C6	Cell line generation services
Biochrom AG	Nov. 2008	PER.C6/ PERMECXIS	Medium Development
Cambrex	Aug. 2004	PER.C6	Medium development
DSM Biologics	Dec. 2002	PER.C6	Therapeutic proteins (including antibodies)
Thermo Fischer Scientific Inc.	Dec. 2003	PER.C6	Medium development
Invitrogen Corp.	Jun. 2003	PER.C6	Medium development
JRH Biosciences Inc.	May 2004	PER.C6	Medium development Recombinant vaccines
KBI Biopharma	Jan. 2009	PER.C6	Cell line generation services
Lonza	Nov.2008	PER.C6/ PERMECXIS	Medium Development
SAFC Pharma	Dec. 2001	PER.C6	Recombinant vaccines & gene therapy products (US)
Sigma-Aldrich Corp.	Dec. 2003	PER.C6	Medium development
Vivante GMP Solutions, Inc.	Jun. 2009	PER.C6	Manufacturing services and gene therapeutics

### Functional Genomics

Partner/licensee	Starting date	Technology	Area
Galapagos Genomics N.V.	Jun. 1999	PER.C6	Genomics



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# Exhibits

## Exhibit

### Number Description

1.1	Deed of Incorporation of the Company (incorporated by reference as Exhibit 3.1 to Crucell N.V.'s amended Registration Statement on Form F-1/A, as filed with the Securities and Exchange Commission on October 24, 2000)
1.2	Amended articles of association (incorporated by reference as Exhibit 1.2 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 13, 2007)
4.1	Summary and Lease Agreement dated November 18, 1998, between IntroGene B.V. and Amboz B.V. (incorporated by reference as Exhibit 4.1 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 28, 2001)
4.2	Summary and Lease Agreement dated November 27, 1997, between IntroGene B.V. and CAM Implants B.V. (incorporated by reference as Exhibit 4.2 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 28, 2001)
4.3	Lease Agreement dated July 1, 2002 between Crucell Holland B.V. and Oppenheim Property Services B.V. (English translation) (incorporated by reference as Exhibit 4.3 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on April 18, 2003)
4.4	Collaboration Agreement dated December 18, 2002 by and between Crucell N.V. and Crucell Holland B.V., and DSM Biologics Holding, Inc., DSM Biologics Company, Inc., and DSM Biologics Company, B.V. (English translation) (incorporated by reference as Exhibit 4.4 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on April 18, 2003) <sup>†</sup>
4.5	Employment Contract dated June 30, 2006 between Crucell Holland B.V. and R.H.P. Brus (incorporated by reference as Exhibit 4.5 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 13, 2007)
4.6	Employment Contract dated June 30, 2006 between Crucell Holland B.V. and Prof. Dr. J. Goudsmit (incorporated by reference as Exhibit 4.6 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 13, 2007)
4.7	Employment Contract dated June 30, 2006 between Crucell Holland B.V. and L. Kruimer (incorporated by reference as Exhibit 4.7 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on June 13, 2007)
4.8	Collaboration and License Agreement dated December 31, 2003 by and between Crucell Holland B.V. and Aventis Pasteur S.A. (now sanofi-pasteur) (incorporated by reference as Exhibit 4.6 to Crucell N.V.'s annual report on Form 20-F, as filed with the Securities and Exchange Commission on February 27, 2004) <sup>†</sup>
4.9	Transaction Agreement dated December 1, 2005 by and between Crucell N.V. and Berna Biotech AG (incorporated by reference as Exhibit 4.9 to Crucell N.V.'s amended annual report on Form 20-F/A, as filed with the Securities and Exchange Commission on June 30, 2006)
4.10	Supply Agreement dated November 12, 2001 and the Letter of Amendment to the same Agreement, dated June 18, 2004 between CSL Limited and Berna Biotech Limited (incorporated by reference as Exhibit 4.10 to Crucell N.V.'s amended annual report on Form 20-F/A, as filed with the Securities and Exchange Commission on December 7, 2007)*

- 4.11 Collaboration Agreement dated April 30, 2001 between Chiron Behring GmbH & Co. and Rhein Biotech N.V. and Green Cross Vaccine Corporation (incorporated by reference as Exhibit 4.11 to Crucell N.V.'s amended annual report on Form 20-F/A, as filed with the Securities and Exchange Commission on December 7, 2007)\*
- 4.12 Employment contract dated September 1, 2007 between Crucell N.V. and C. de Jong (incorporated by reference as exhibit 4.12 to Crucell N.V.'s Annual Report on Form 20-F, as filed with the securities and exchange commission on April 22, 2009)
- 4.13 Equity Purchase Agreement dated September 28, 2009 between JHC Nederland B.V. and Crucell N.V.\*
- 4.14 Shareholder Agreement dated September 28, 2009 between JHC Nederland B.V. and Crucell N.V.\*
- 8.1 List of subsidiaries of Crucell N.V.
- 12.1 Certification of CEO pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
- 12.2 Certification of CFO pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
- 13.1 Certification of CEO and CFO pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
- 99.1 Crucell Code of Conduct (incorporated by reference as exhibit 99.1 to Crucell N.V.'s Annual Report on Form 20-F, as filed with the securities and exchange commission on April 22, 2009)

Confidential treatment has been granted with respect to portions of the exhibit indicated by a dagger (†). The omitted portions have been filed separately with the Securities and Exchange Commission. \* Confidential treatment requested as to certain portions, which portions have been filed separately with the Securities and Exchange Commission by Crucell N.V.



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