CRUCELL N.V.

a public limited liability company (*naamloze vennootschap*) incorporated in the Netherlands with its statutory seat (*statutaire zetel*) in Leiden, the Netherlands

Admission to trading of 14,626,984 newly issued ordinary shares with a nominal value of € 0.24 per share

On 28 September 2009 (the **Issue Date**) we issued a total amount of 14,626,984 Shares (as defined below) (the **New Shares**) at a price of € 20.63 each (the **Issue Price**) to JHC Nederland B.V. (the **Investor**) by means of a private placement (the **Issuance**).

In this document (the **Prospectus**) **Shares** means ordinary shares in our capital with a nominal value of 0.24 each.

Our business and any investments in our Shares involve significant risks. These risks are described under Chapter 2 "Risk Factors" beginning on page 8 of this Prospectus.

Our Shares (other than the New Shares) are listed and traded on Euronext Amsterdam by NYSE Euronext (**Euronext Amsterdam**) under the symbol CRXL and ISIN CODE NL0000358562.

Application has been made to NYSE Euronext to admit the New Shares to trading on Euronext Amsterdam. We expect that trading in the New Shares on Euronext Amsterdam will commence on or about 30 October 2009 (the **Listing Date**).

This Prospectus does not constitute an offer to sell, or a solicitation of an offer to buy, any of the New Shares or any other securities issued by the Company.

The Issue Price has been determined by taking the average of the daily volume-weighted average price of the Shares listed on Euronext Amsterdam for each of the 35 (thirty-five) consecutive Euronext Amsterdam trading days immediately preceding the Issue Date (the **Original Market Price**) plus a premium of 30% over the Original Market Price.

This Prospectus constitutes a prospectus for the purposes of Article 3 of Directive 2003/71/EC (the **Prospectus Directive**) and has been prepared in accordance with Chapter 5.1 of the Dutch Financial Supervision Act (*Wet op het financieel toezicht*) and in accordance with the rules promulgated thereunder (the **Financial Supervision Act**). This Prospectus has been approved by the Netherlands Authority for the Financial Markets (*Stichting Autoriteit Financiële Markten*) (**AFM**).

This Prospectus is dated 28 October 2009.

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1 SUMMARY

The following information should be read as an introduction to this Prospectus only. This summary is not complete and does not contain all information that should be considered in connection with any decision to invest in the Shares. Any decision to invest in the Shares should be based on a consideration of this Prospectus and the information incorporated by reference into this Prospectus as a whole and not just this summary.

Where a claim relating to the information contained in, or incorporated by reference into, this document is brought before a court in a Member State, the claimant might, under the national legislation of the Member State, have to bear the costs of translating this document or any document incorporated by reference herein before the legal proceedings are initiated. Civil liability attaches to the Company, which is responsible for this summary, but only if this summary (or any translation of this summary) is misleading, inaccurate or inconsistent when read together with the other parts of this document (including information incorporated by reference herein).

1.1 Summary of the business

We are a fully integrated biopharmaceutical company. We focus on developing, producing and marketing products that combat 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 the volume of global travel which boosts the potential for spreading diseases across borders. Currently we are combating 12 major infectious diseases with our armamentarium of marketed vaccines. In 2008, we sold more than 100 million vaccine doses in more than 80 countries throughout the world, which makes us the largest independent vaccine player in the world. Our product portfolio consists of three distinct focus areas: paediatric, travel/endemic and respiratory. We are the largest independent vaccine company in the world. The sustainability of our business is demonstrated by our solid balance sheet and strong cash position which allows us to invest significantly in research and development (**R&D**). Our research efforts today are focusing on developing vaccines and antibodies that address unmet medical needs and infectious diseases. Our research efforts are bolstered by our range of technologies, which play a critical role in our development programs. Our discovery programs include a number of potential products against infectious diseases that are in the clinical stage of development. 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.

1.2 Summary of the strategy

We have a clearly defined vision: to bring innovation to global health by discovering, developing, manufacturing, and marketing products that protect people from illness and death caused by infectious diseases. We develop products that address currently unmet medical needs, particularly in the field of infectious diseases. Infectious diseases are responsible for almost one-fifth of the total number of deaths that occur each year, according to the latest World Health Organization (**WHO**) statistics (source: World Health Statistics 2008). Overall, they rank second after cardiovascular disease as the leading cause of death worldwide. The vast majority of people who die from infectious diseases live in the world's poorest and most densely populated countries, although increased global travel and climate change are expanding the reach of infectious pathogens. The full impact of infectious diseases has to be measured not only by the millions of fatal cases, but also in terms of the much larger burden of illness and suffering, lost productivity and even ruined holidays. Children and the elderly are especially vulnerable to infectious diseases, with the latter forming a growing group due to the ageing population. According to the WHO, about 25 million deaths that occur each year in children under five are caused by diseases that can be prevented with vaccines. 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 used to produce high-value biotech products in scalable and cost efficient ways. This combination of markets we operate in, technological knowledge and quality marketed products, positions us to be a major player in the multi-billion dollar biopharmaceutical arena. We aim for financial profitability, but also to bring the greatest possible benefit to human health worldwide. The approach we have chosen to achieve this is essentially different from that of our biotechnology peers or traditional pharmaceutical companies. Whereas many others focus on treating illness, we focus on its prevention. And whereas most of the money currently spent on pharmaceutical research is directed towards finding solutions for lifestyle-related illnesses of the developed world, we have developed a truly global healthcare strategy. Our existing and pipeline products are designed to meet the long underestimated – and still significantly unmet – need for vaccines and antibodies in developing countries and emerging economies, as well as the industrialized world. For a company of our size, we invest relatively heavily in R&D: our R&D expenditures in 2008 were € 70 million.

1.3 Summary of the risk factors

Strategic risk factors

- 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 results may fluctuate as a result of seasonality.

- The revenues related to our current or prospective partners or licensees could cease to be realized due to a business combination or insolvency of any one of them.

- We may not receive all royalty payments owed to us by licensees.

- Competition and pricing pressures may have a material adverse effect on our business, results of operations and financial condition.

Operational risk factors

- Any or all of our products and those of our licensees and partners at any stage of development or even after market introduction might fail and could have a material adverse effect on our business and prospects.

- 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.

- Interrupted product supply as a result of a worldwide flu pandemic.

- If regulatory authorities do not approve our new products or other products developed using our technologies, or if they subsequently revoke their approval or impose fines or restrictions upon the manufacture and sale of our products, such event may have a material adverse impact on our business, financial condition, results of operations and prospects.

- Our success depends on our ability to obtain and maintain intellectual property (**IP**) rights held by us and third parties and the value of such rights is complex and uncertain.

- We have a significant product liability exposure which could have a material adverse effect on our business where liabilities could even exceed our total assets. We may not be able to obtain sufficient product liability insurance coverage, which could have a material adverse effect on our results and operations

- 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.

- We are subjected to the risk of civil damages and significant adverse publicity related to the use of hazardous biological materials.

- We may be in breach of competition laws.

Financial risk factors

- We have a track record of substantial use of capital which could continue in the future.

- The weakness in the global economy could negatively affect our business.

- We are subjected to significant foreign currency risks.

- Tax law changes may adversely affect our profitability and the sale of our products.

Compliance and other

- The use of genetic technology may raise ethical, legal and/or social issues that could have material adverse consequences for our business

Risks related to the Shares

- Our Articles of Association contain protective measures which may have the effect of delaying, deterring or preventing a change of control and/or preventing Shareholders from selling their Shares or ADSs at a premium to the market price.

- Future sales, or the possibility of future sales, of a substantial number of Shares (including New Shares) could depress the market price of the Shares.

- We may in the future seek to raise capital by conducting equity offerings which may dilute investors' shareholding in us.

- If securities or industry analysts do not publish research or reports about our business, or if they change their recommendations regarding the Shares adversely, the market price and trading volume of the Shares could decline.

- American and other non-Dutch holders of our Shares may not be able to exercise pre-emption rights.

- Shareholders may have difficulties protecting their interests as shareholders as we are a Dutch limited liability company.

- Our share price can be volatile.

1.4 Summary of the terms of the Issuance

Issuing entity	Crucell N.V.
Issuance	The Issuance constituted a private placement to the Investor of the New Shares (being 14,626,984 Shares) at a price of € 20.63 each (the **Issue Price**) (totalling an amount of € 301,754,679.90).
Issue Date	28 September 2009.
Investor	JHC Nederland B.V.
Shareholder Agreement	Concurrently with and in relation to the Issuance, we entered into a shareholder agreement with Investor (the **Shareholder Agreement**) which defines the rights and obligations of Investor as a shareholder of the Company. For further details, please refer to Chapter 12 "Major Shareholders".
Collaboration Agreements	Concurrently with and in relation to the Issuance, we entered into the Collaboration Agreements. For further details, please refer to Chapter 10 "Business Overview".
Shares issued at the date of this Prospectus	81,267,355 Shares (including the New Shares and treasury shares).
Share ownership	Pursuant to information derived from the register of the Financial Supervision Act maintained by the AFM as per the date of this Prospectus 18% of our Shares are held by the Investor and 8.60% by A. van Herk B.V.
Listing Date	On or about 30 October 2009.
Use of Proceeds	We intend to use the net proceeds of the Issuance to execute the research and development plans with the Affiliates of the Investor, further development of our clinical and pre-clinical programs, capital expenditures, acquisitions, alliances and for general corporate purposes.
Dividends	We do not anticipate paying any dividends for the foreseeable future.
Voting rights	A Share entitles its holder to cast one vote in each General Meeting.
Share trading information	ISIN CODE: NL0000358562 Common Code: 11907164 Amsterdam Security Number: 35856 Euronext Amsterdam symbol: CRXL SWX Swiss Exchange symbol: CXL NASDAQ symbol: CRXL

1.5 Summary of the consolidated financial information

The summary consolidated financial information set forth below should be read in conjunction with the Chapters 7 "Selected Financial Data" and 8 "Operating and Financial Review", our annual consolidated financial statements and their related notes and our unaudited condensed interim reports that are incorporated by reference in this Prospectus. The consolidated financial information has been extracted

from our annual consolidated financial statements that have been audited by Deloitte Accountants B.V., independent auditors, and the unaudited condensed interim reports.

Our consolidated financial statements, from which the summary consolidated financial information set forth below has been derived, were prepared in accordance with IFRS. The summary consolidated financial information set forth below may not contain all of the information that is important to you.

In thousands of euro	**Year Ended 31 December**			**6 months period ended June 30**	
	Audited			**Unaudited**	
	2008	**2007**	**2006**	**2009**	**2008**
Product sales	226,055	177,569	103,918	129,566	83,910
License revenues	30,202	12,211	16,955	7,978	10,755
Service fees	10,900	14,006	10,694	5,362	4,302
Total revenues	**267,157**	**203,786**	**131,567**	**142,906**	**98,967**
Cost of product sales	(138,790)	(124,557)	(83,518)	(78,393)	(58,760)
Cost of service and license fees	(6,965)	(10,327)	(6,971)	(4,893)	(2,603)
Total cost of goods sold	**(145,755)**	**(134,884)**	**(90,489)**	**(83,286)**	**(61,363)**
Gross margin	**121,402**	**68,902**	**41,078**	**59,620**	**37,604**
Government grants	5,380	7,086	6,901	2,027	2,103
Other income	10,772	2,244	2,455	7,480	6,458
Total other operating income	**16,152**	**9,330**	**9,356**	**9,507**	**8,561**
Research and development	(70,229)	(63,995)	(67,606)	(31,239)	(33,455)
Selling, general and administrative	(64,350)	(61,752)	(46,732)	(32,337)	(29,956)
Restructuring	-	-	(3,120)	-	5,153
Reversal of impairment/(impairment)	4,888	(171)	(30,416)	-	-
Total other operating expenses	**(129,691)**	**(125,918)**	**(147,874)**	**(63,576)**	**(58,258)**
Operating profit (loss)	**7,863**	**(47,686)**	**(97,440)**	**5,551**	**(12,093)**
Financial income and expense	(2,662)	1,378	1,747	(2,843)	(2,093)
Result investments non-consolidated companies	(128)	(996)	(1,956)	225	(183)
Result disposal of non-consolidated companies	1,570	2,186	-	-	-
Disposal of subsidiaries	(367)	-	-	-	-
Profit (loss) before tax	**6,276**	**(45,118)**	**(97,649)**	**2,933**	**(14,369)**
Income tax	8,310	2,208	10,451	(4,573)	(1,515)
Profit / (loss) for the year	**14,586**	**(42,910)**	**(87,198)**	**(1,640)**	**(15,884)**
Attributable to:					
Equity holders of the parent	14,586	(42,910)	(86,946)	(1,640)	(15,884)
Minority interest	-	-	(252)	-	-
Weighted average shares outstanding – basic	65,593	65,103	57,064	66,338	65,478
Weighted average shares outstanding – diluted	66,315	65,103	57,064	67,934	65,478

In thousands of euro	Year Ended 31 December			Six months period ended June 30	
	Audited			Unaudited	
	2008	2007	2006	2009	2008
Selected data from statements of financial position					
Cash and cash equivalents	170,969	163,248	157,837	121,591	106,883
Current assets excluding cash	151,349	140,014	159,234	192,686	156,066
Current liabilities	118,301	114,742	90,252	110,285	88,520
Shareholders' equity	453,492	441,103	497,886	463,155	413,322
Selected cash flow data					
Cash flows (used) from operating activities	(254)	22,194	(53,954)	(26,945)	(51,944)
Cash flows from (used) in investing activities	(8,907)	(24,241)	23,159	(17,491)	(52)
Cash flows from (used) in financing activities	16,626	11,244	78,371	(4,751)	(4,070)

2 RISK FACTORS

Prospective investors should carefully consider the risk factors set out below, together with the other information contained in this Prospectus, before making an investment decision with respect to investing in our Shares. If any of the following risks actually materializes, our business, prospects, financial condition or results from operations could be materially adversely affected. In that case, the value of our Shares could decline and investors could lose all or part of the value of their investments. All of these risk factors are contingencies which may or may not occur. We may face one or more of the risks described below simultaneously.

The risks we face are not limited to the risks listed below. 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

Prospective investors should carefully review the entire Prospectus and should form their own views before making an investment decision with respect to our Shares. Before making an investment decision with respect to any of our Shares, prospective investors should also consult their own financial, legal and tax advisers to carefully review the risks associated with an investment in our Shares and consider such an investment decision in light of the prospective investor's personal circumstances.

2.1 Strategic risk factors

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 results may fluctuate as a result of seasonality

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 seven vaccines, namely Quinvaxem, Hepavax-Gene and MoRu-Viraten (paediatric vaccines), Inflexal V (influenza), Dukoral, Epaxal and Vivotif (travel vaccines). The aggregated revenues for our core product portfolio represent a significant part of our total product sales. The sales to our largest customers, which are in the paediatric vaccines area, represented a considerable part of our net product sales. In particular, we are highly dependent on sales of Quinvaxem and Inflexal 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.

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

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

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.

We may not receive all royalty payments owed to us by licensees

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. In addition, our licensees may have difficulties making payments to us given the current economic climate or other factors. We may also incur significant expenses in collecting royalty payments, or in some instances, may not succeed in collecting these payments at all. The downfall of the revenues related to our current and prospective partners and licensees could materially effect our business.

Competition and pricing pressures may have a material adverse effect on our business, results of operations and financial condition

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 pricing pressures from competition with other products on the market. Pricing pressures 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. Increased competition from these products could result in further pricing pressure on Quinvaxem and have a substantially negative impact on our revenues.

We experience pricing pressures in the public markets for our products, which 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. Pricing pressures may have a material adverse effect on our business, results of operations and financial condition.

2.2 Operational risk factors

Any or all of our products and those of our licensees and partners at any stage of development or even after market introduction may fail and could have a material adverse effect on our business and prospects

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 shown sufficiently safe or effective to be brought to market, or could otherwise fail to receive 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. 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 R&D. 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 a certain extent, we are dependent on third parties with which we cooperate to perform clinical trials of our products. If we fail to adequately manage the work of these third parties, a regulatory authority may determine that these third parties have not complied with applicable regulations and therefore may not approve a product candidate of ours.

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.

Supply interruptions, product recalls or inventory losses caused by unforeseen events such as defects in the manufacturing process, regulatory actions, distribution interruptions or adverse changes to our existing supplier relationships, may reduce sales, delay the launch of new products and adversely affect our operating results and financial condition

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.

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, labour 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 or marketing delays due to new validation activities to demonstrate similarities, or differences

in comparability studies between old and 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 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 any 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 South Korea is our sole production source of the Quinvaxem vaccine. As such, we are vulnerable to any event that interrupts, reduces or slows production of Quinvaxem at that facility. We intend to relocate our Quinvaxem operations to another site in South 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, enabling a smooth transition to the new production facility; however, there can be no assurance that there will be no delay in the transition process.

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. Any interruption or termination of these supply relationships may have adverse effects on our ability to manufacture and sell products, particularly if we are unable to source new supplies of the same materials or adapt our technologies and manufacturing processes to use different starting materials in a timely manner. 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.

Interrupted product supply as a result of a worldwide flu pandemic

There is an increased perception in the market that companies may not be able to acquire certain resources as these may become limited in supply as the worldwide flu pandemic evolves. The impact on our antigen sourcing is assessed to be limited in the coming six months.

If regulatory authorities do not approve our new products or other products developed using our technologies, or if they subsequently revoke their approval or impose fines or restrictions upon the manufacture and sale of our products, such event may have a material adverse impact on our business, financial condition, results of operations and prospects

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 (**EMEA**), the European Commission or other non-governmental bodies such as the 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.

Regulatory requirements could make product development based on new technologies highly uncertain because regulatory review of the underlying technologies is generally required.

If regulatory authorities do not approve our new products or other products developed using our technologies, or if they subsequently revoke their approval or impose fines or restrictions upon the manufacture and sale of our products, such event 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.

Our success depends on our ability to obtain and maintain intellectual property rights held by us and third parties and the value and protection of such rights is complex and uncertain

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 GlaxosmithKline (**GSK**) and us or GSK and our supplier of that component. However, neither we nor our supplier are believed to have infringed or be infringing that particular 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. See Chapter 10.9 “Business Overview - Intellectual property” for further details on patent enforcement and proceedings.

We also endeavour to protect our proprietary technologies, processes, know-how and data by entering into confidentiality agreements with our employees, consultants, partners and certain contractors. We have no assurance that these agreements or other trade secret protections will provide meaningful protection to us.

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.

We have a significant product liability exposure which could have a material adverse effect on our business where liabilities could even exceed our total assets. We may not be able to obtain sufficient product liability insurance coverage, which could have a material adverse effect on our results and operations

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 it cannot be assured that such additional insurance will not be prohibitively expensive, or that it will 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 which could have a material adverse effect on our results and operations.

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, there can be no assurance as to the outcome of these matters and we could incur judgments or enter into settlements of claims that could have a material adverse effect on our results of operations.

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.

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 labour costs and materially affect our prospects.

We are subjected to the risk of civil damages and significant adverse publicity related to the use of hazardous biological materials

Our manufacturing, R&D processes involve the controlled use of hazardous biological materials.

Certain of our 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, 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.

We may be in breach of 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.

2.3 Financial risk factors

We have a track record of substantial use of capital, which could continue in the future

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. We also have incurred accumulated net operating losses since our incorporation.

Although we generated positive cash flow in 2008, 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 favourable 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. This would likely adversely affect our overall results.

The weakness in the global economy could negatively affect our business

The weakness of the global economy is a challenge for many companies. The ongoing financial crises adversely affected businesses in many industries and geographical areas all over the world. Except for our travel portfolio, we are relatively unaffected by the financial crisis. We note that international travel

is reduced by the financial crisis as well as the global pandemic, which will in turn negatively affect the number of travel vaccinations. We expect the effects on our travel portfolio to have a limited effect on our overall profitability and liquidity. We do not expect that the weakness of the global economy will significantly impact our liquidity or our ability to derive revenues from our operations. We do note that there can be no assurance that our liquidity will not be affected by recent and possible future changes in global financial markets and global economic conditions.

We are subjected to significant foreign currency risks

The majority of our total revenues are 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 recent 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.

During the first half of 2009, our margins were negatively affected by currency fluctuations; the US dollar decreased in value compared to the euro. As per 30 June 2009 the euro/US dollar rate is 1.40, which is below our guidance rate of euro/US dollar 1.35. Compared to 2008, the Swiss Franc strengthened against the euro, which had a negative currency effect on our results as we produce Inflexal, Epaxal and Vivotif at our Swiss facilities. The Korean Won experienced significant volatility over the past year compared to the US dollar, which is relevant as we produce Quinvaxem and Hepavax-Gene in our South Korean facilities. In the remainder of 2009, our results will be further impacted by currency movements.

Tax law changes may adversely affect our profitability and the sale of our products

We are subject to European tax law as well as to the tax laws of the countries in which we operate. 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 Chapter 8.13 “Operating and Financial Review - Corporate income taxes” for further details on taxation.

2.4 Compliance and other

The use of genetic technology may raise ethical, legal and/or social issues that could have material adverse consequences for our business

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.

2.5 Risks related to the Shares

Our Articles of Association contain protective measures which may prevent corporate action and/or shareholder transactions that might be in the best interests of the Company or the Shareholders

and may have the effect of delaying, deterring or preventing a change of control and/or preventing Shareholders from selling their Shares or ADSs at a premium to the market price

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.

Future sales, or the possibility of future sales, of a substantial number of Shares (including New Shares) could adversely affect the market price of the Shares

Following the issue, sales of a substantial number of Shares (including New Shares) in the public market, or the perception that such sales may occur, could adversely affect the market price for the Shares. Although the Investor has agreed to certain restrictions on the sale or other disposition of New Shares for a three months period as of the Issue Date, the New Shares (or ADSs acquired in exchange for such Shares) held by the Investor upon expiry of such period will thereafter be freely transferable.

We may in the future seek to raise capital by conducting equity offerings, which may dilute investors' shareholding in us and may have a negative impact on the trading price of the Shares

The Management Board, subject to the approval of the Supervisory Board, has been designated as the authorised body to issue Shares for a period up to and including 30 November 2010. Pursuant to this designation by the General Meeting, the Management Board may resolve to issue Shares up to 15% of the outstanding Shares, increased by another 15% in the event of a merger, cooperation or an acquisition involving us. We may seek to raise capital in the future through public or private debt or equity financings by issuing additional Shares or other shares, debt or equity securities convertible into or exchangeable or excisable for Shares or rights to acquire these securities and exclude the pre-emptive rights pertaining to the then outstanding Shares. Any additional capital raised through the issue of additional Shares may dilute an investor's shareholding interest in us. Furthermore, any additional financing we may need may not be available on terms favourable to us or at all, which could adversely affect our future plans. Any additional offering of shares by us, or the public perception that an offering may occur, could also have a negative impact on the trading price of the Shares and could increase the volatility in the trading price of the ordinary shares.

If securities or industry analysts do not publish research or reports about our business, or if they change their recommendations regarding the Shares adversely, the market price and trading volume of the Shares could decline

The market for the Shares will be influenced by the research and reports that securities or industry analysts publish about Crucell. If one or more of the analysts who cover Crucell, or the industry in which it operates, downgrade the Shares, the market price of the Shares would be likely to decline. If one or more of these analysts ceases coverage of Crucell or fails to regularly publish reports on Crucell, Crucell could lose visibility in the financial markets, which could cause the market price of the Shares or trading volume to decline.

American and other non-Dutch holders of our Shares may not be able to exercise pre-emption rights

In the event of an increase in our share capital, holders of our Shares are generally entitled to certain pre-emption rights unless these rights are excluded by a resolution of the General Meeting or a meeting of the Management Board if so delegated by the General Meeting. However, US holders of our 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 difficulties 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.

Our Share price can be volatile

Our Shares and ADSs may have a highly volatile trading price. Shareholders may not be able to resell their 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. Our Shares are listed on Euronext Amsterdam and SWX Swiss Exchange, and our ADSs are listed on the NASDAQ Global Select Market. 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 Share or ADSs 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 Shares and ADSs, regardless of our performance.

3 IMPORTANT INFORMATION

3.1 Responsibility Statement

Potential investors should rely on the information contained in this Prospectus and any supplement to this Prospectus within the meaning of Article 5:23 of the Financial Supervision Act. Potential investors should not assume that the information in this Prospectus is accurate as of any date other than the date of this Prospectus. No person is or has been authorised to give any information or to make any representation in connection with the admission of the New Shares to trading on Euronext Amsterdam, other than as contained in this Prospectus. If any information or representation not contained in this Prospectus is given or made, the information or representation must not be relied upon as having been authorised by the Company. The delivery of this Prospectus at any time after the date hereof will not, under any circumstances, create any implication that there has been no change in the our affairs since the date hereof or that the information set forth in this Prospectus is correct as of any time since its date.

The Company accepts responsibility for the information contained in this Prospectus. The Company declares that it has taken all reasonable care to ensure that, to the best of its knowledge, the information contained in this Prospectus is in accordance with the facts and contains no omission likely to affect its import.

In this Prospectus, **Crucell**, **we**, the **Group**, **our**, **us** and similar terms refer to Crucell N.V. and, where appropriate, any or all of its subsidiaries. The term Company refers to Crucell N.V.

3.2 Presentation of financial and other information

The consolidated financial information in this Prospectus for the years ended 31 December 2006, 31 December 2007 and 31 December 2008 is extracted from the annual consolidated financial statements of the Company (including the comparative figures and notes thereto) that have been prepared in accordance with IFRS and that have been audited by Deloitte Accountants B.V. The unaudited consolidated interim financial statements in relation to the six months ended on 30 June 2008 and 30 June 2009 have been prepared in accordance with IAS 34 'Interim Financial Reporting'.

The Company's historical consolidated financial statements include:

- the audited consolidated financial statements of the Company prepared in accordance with IFRS as at and for the year ended 31 December 2006;
- the audited consolidated financial statements of the Company prepared in accordance with IFRS as at and for the year ended 31 December 2007;
- the audited consolidated financial statements of the Company prepared in accordance with IFRS as at and for the year ended 31 December 2008; and
- the condensed consolidated interim financial information of the Company prepared in accordance with IFRS for the six months ended 30 June 2009 and the six months ended 30 June 2008,

in each case together with the respective notes thereto.

Capitalization and indebtedness information for the Company in this Prospectus is extracted from the unaudited consolidated interim financial statements in relation to the six months ended on 30 June 2009.

Certain figures contained in this Prospectus, including financial information, have been subject to rounding adjustments. Accordingly, in certain instances the sum of the numbers in a column or a row

of a table contained in this Prospectus may not conform exactly to the total figure given for that column or row.

All references in this Prospectus to "euro" or "€" are to the currency introduced at the start of the third stage of the Economic and Monetary Union, pursuant to the Treaty establishing the European Economic Community, as amended by the Treaty on the EU. All references to "US dollar" or "$", are to the lawful currency of the United States. See "Exchange Rates".

3.3 Exchange rates

We publish our historical consolidated financial statements in euro. The exchange rates below are provided solely for information and convenience. No representation is made that the euro could have been, or could be, converted into US dollar at these rates.

US dollar

The table below shows the high, low, average and end period exchange rates expressed in US dollar per € 1.00 for the years given as computed using the noon buying rate in New York City for cable transfers in foreign currencies as certified for customs purposes by the Federal Reserve Bank of New York (the **Noon Buying Rate**) during the period indicated.

Year ended 31 December,	**High**	**Low**	**Average[(1)]**	**End of Period**
	US dollar per euro			
2005	1.37	1.16	1.25	1.18
2006	1.34	1.18	1.26	1.32
2007	1.50	1.29	1.37	1.47
2008	1.60	1.23	1.47	1.41

(1) The average of the Noon Buying Rates on the last business day of each month during the relevant period.

The table below shows the rates as used by the Company expressed in US dollar per € 1.00 for each month during the first six months of 2009.

	High	**Low**
	US dollar per euro	
January 2009	1.41	1.28
February 2009	1.32	1.25
March 2009	1.37	1.25
April 2009	1.36	1.29
May 2009	1.41	1.32
June 2009	1.43	1.37

On 28 September 2009, the dollar rate used for the euro was € 1.00 = $ 1.46960.

3.4 Incorporation by reference

The following documents, which have previously been published and have been filed with the AFM and/or the Chamber of Commerce, shall be incorporated in, and form part of, this Prospectus and are available for inspection as provided in Chapter 16.1 "General Information - Available information":

(a) the audited consolidated annual financial statements and the auditor's report for the financial year ended 31 December 2006 (the **2006 Financial Statements**) including the information set out on the following pages:

Consolidated Income Statement	Page 59
Consolidated Balance Sheet	Pages 60 and 61
Consolidated Cash Flow Statement	Pages 64 and 65
Consolidated Statements of Changes in Equity	Page 62 and 63
Accounting Principles and Notes to the consolidated financial statements	Pages 66 - 123
Company Income Statement	Page 132
Company Balance Sheet	Page 131
Accounting Principles and Notes to the Company financial statements	Page 132-134
Consolidated and Company Auditor's Report	Pages 137 and 138

(b) the audited consolidated annual financial statements and the auditor's report for the financial year ended 31 December 2007 (the **2007 Financial Statements)** including the information set out on the following pages:

Consolidated Income Statement	Page 132
Consolidated Balance Sheet	Page 133
Consolidated Cash Flow Statement	Page 135
Consolidated Statements of Changes in Equity	Page 134
Accounting Principles and Notes to the consolidated financial statements	Pages 136 - 173
Company Income Statement	Page 174
Company Balance Sheet	Page 174
Accounting Principles and Notes to the Company financial statements	Page 175
Consolidated and Company Auditor's report	Page 178

(c) the audited consolidated annual financial statements and the auditor's report for the financial year ended 31 December 2008 (the **2008 Financial Statements**, together with the 2006 Financial Statements and the 2007 Financial Statements the **Audited Financial Statements**) including the information set out on the following pages:

Consolidated Income Statement	Page 125
Consolidated Balance Sheet	Page 126
Consolidated Cash Flow Statement	Page 128
Consolidated Statements of Changes in Equity	Page 127
Accounting Principles and Notes to the consolidated financial statements	Pages 129 - 170
Company Income Statement	Page 171
Company Balance Sheet	Page 171
Accounting Principles and Notes to the Company financial statements	Pages 172 and 173
Consolidated and Company Auditor's Report	Page 176

(d) The unaudited consolidated interim financial statements as at and for the first half year ended 30 June 2008 (the **H1 2008 Statements**) including the information set out on the following pages:

Consolidated Statement of Operations	Page 13
Consolidated Balance Sheets	Page 14
Consolidated Cash Flow Statement	Page 15

(e) The unaudited consolidated interim financial statements as at and for the first half year ended 30 June 2009 (the **H1 2009 Statements** and, together with the H1 2008 Statements, the **Semi-Annual Financial Statements**) including the information set out on the following pages;

Condensed consolidated statements of income	Page 20
Condensed consolidated statements of financial position	Page 21
Condensed Consolidated Statements of Cash Flow	Page 22
Condensed consolidated statements of comprehensive income	Page 23
Condensed consolidated statement of changes in equity	Page 24
Accounting Principles and Notes to the consolidated financial statements	Page 25 -32

Please note that the references direct to the pages of the annual reports for the financial years 2006, 2007 and 2008 in which the Audited Financial Statements have been included and the pdf versions of the press releases in which the Semi-Annual Financial Statements have been included. The Semi-Annual Financial Statements are not audited nor reviewed.

(f) the articles of association of the Company as they read on the date of this Prospectus (**the Articles of Association**).

The Audited Financial Statements, the Semi-Annual Financial Statements and the Articles of Association shall be incorporated in, and form part of, this Prospectus and can be obtained free of charge on the Company's website at www.crucell.com.

Any information that is incorporated by reference into documents, which in turn are incorporated into this Prospectus, is not incorporated by reference in this Prospectus.

If, prior to the commencement of trading of the New Shares on Euronext Amsterdam, a significant new development occurs in relation to the information contained in the Prospectus or a material mistake or inaccuracy is found in the Prospectus that may affect the assessment of the Shares, a supplement to this Prospectus will be published which is to be approved by the AFM, in accordance with Article 5:23 of the Financial Supervision Act.

Statements contained in any such supplement (or contained in any document incorporated by reference therein) shall, to the extent applicable (whether expressly, by implication or otherwise), be deemed to modify or supersede statements contained in this Prospectus or in a document which is incorporated by reference in this Prospectus. Any statement so modified or superseded shall not, except as so modified or superseded, constitute a part of this Prospectus.

Investors should rely only on the information that is provided in this Prospectus or incorporated by reference into this Prospectus. No other documents or information, including the contents of the Company's website or of websites accessible from hyperlinks on the Company's website, form part of, or are incorporated by reference into, this Prospectus.

3.5 Forward-looking statements

The statements contained in this Prospectus that are not historical facts are "forward-looking statements". This Prospectus contains forward-looking statements in Chapter 2 "Risk Factors", Chapter 8 "Operating and Financial Review" , Chapter 9 "Industry Overview", and Chapter 10 "Business Overview", which are based on the Company's beliefs and projections and on information currently available. These forward-looking statements are subject to a number of risks and uncertainties, many of which are beyond the Company's control and all of which are based on the Company's current beliefs and expectations about future events. Forward-looking statements are typically identified by the use of forward-looking terminology such as "believes", "expects", "may", "will", "could", "should", "intends", "estimates", "plans", "assumes", "anticipates", "annualised", "goal", "target" or "aim" or the negative thereof or other variations thereon or comparable terminology, or by discussions of strategy that involve risks and uncertainties.

Forward-looking statements involve inherent risks and uncertainties and speak only as of the date they are made. The Company undertakes no duty to and will not necessarily update any of the forward-looking statements in light of new information or future events, except to the extent required by applicable law. A number of important factors could cause actual results or outcomes to differ materially from those expressed in any forward-looking statement as a result of risks and uncertainties facing the Company and its subsidiaries. Please refer to Chapter 2 "Risk Factors" for more information.

3.6 Enforcement of civil liabilities

The ability of an overseas Shareholder to bring an action against the Company may be limited under law. The Company is a public limited liability company incorporated in the Netherlands. The rights of holders of Shares are governed by Dutch law and by the Articles of Association. These rights differ from the rights of shareholders in US corporations and some other non-Dutch corporations.

An overseas Shareholder may not be able to enforce a judgment against some or all of the directors and the Company's management. The majority of the directors and management are residents of the Netherlands. Consequently, it may not be possible for an overseas Shareholder to effect service of process upon the directors and the Company's management within the overseas Shareholder's country of residence. In addition, it may not be possible to enforce against the directors and the Company's management judgments of courts of the overseas Shareholder's country of residence based on civil liabilities under that country's securities laws. There can be no assurance that an overseas Shareholder will be able to enforce any judgments in civil and commercial matters or any judgments under the securities laws of countries other than the Netherlands against the directors or the Company's management who are residents of the Netherlands or countries other than those in which judgment is made. In addition, Dutch or other courts may not impose civil liability on the directors or the Company's management in any original action based solely on the foreign securities laws brought against the Company or the directors in a court of competent jurisdiction in the Netherlands or other countries.

3.7 Market and industry data

Market and industry data and other statistical information used throughout this Prospectus are based on a number of sources, including independent industry publications, government publications, reports by market research firms or other published independent sources (together the **Independent Sources**). Some data is based on good faith estimates of the Company, which are derived in part from review of internal surveys of the Company, as well as the Independent Sources. Although the Company believes the Independent Sources are reliable, the Company has not independently verified the information and cannot guarantee its accuracy and completeness.

The information in this Prospectus that has been sourced from third parties has been accurately reproduced and, as far as the Company is aware and able to ascertain from the information published by that third party, no facts have been omitted which would render the reproduced information inaccurate or misleading.

4 DIVIDEND POLICY

We have not paid any dividends during the last three financial years.

We currently intend to retain future earnings, if any, to finance the growth and development of our business. As a result we do not anticipate paying any dividends for the foreseeable future 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 and its subsidiaries. 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 ADSs will be entitled to receive payments in US dollar in respect of dividends on the underlying Shares in accordance with a deposit agreement dated 26 October 2000 between The Bank of New York Mellon, as depository, and us.

See Chapter 14.4 "Share Capital and Corporate Governance - Dividends and other distributions" for further details.

5 USE OF PROCEEDS

The proceeds of the Issuance are € 301,754,679.90. We expect the costs related to the Issuance to be approximately € 1.2 million. We expect the net cash proceeds of the Offering to be approximately € 300.5 million.

We intend to use the net proceeds of the Issuance to execute the research and development plans with the Investor and its Affiliates, further development of our clinical and pre-clinical programs, capital expenditures, acquisitions, alliances and for general corporate purposes.

6 CAPITALIZATION AND INDEBTEDNESS

The table below sets forth our unaudited consolidated cash and cash equivalents, capitalization and indebtedness as of 30 June 2009, on an actual basis, incorporating the proceeds of the New Shares. The financial information in the table below has been extracted or derived from our H1 2009 Statements which have not been audited or reviewed. You should read this table together with our audited consolidated financial statements incorporated by reference in this Prospectus, as well as the information under Chapter 8 "Operating and Financial Review". The table below is prepared for illustrative purposes only and, because of its nature, may not give a true picture of our financial condition following the Issuance.

In thousands of euro	**As of June 30, 2009** (unaudited)	**Adjustment for the proceeds of new shares** (unaudited)	**Estimated balances after the transaction** (unaudited)
Total Current Debt			
Guaranteed	0	0	0
Secured [(1)]	3,253	0	3,253
Unguaranteed / Unsecured	14,193	0	14,193
Total Non-Current Debt			
Guaranteed	0	0	0
Secured [(1)]	32,168	0	32,168
Unguaranteed / Unsecured	0	0	0
Total Indebtedness	**49,614**	**0**	**49,614**
Share capital ordinary shares	15,975	3,510	19,485
Share premium	754,241	228,569	982,810
Net unrealized gains reserve	7,405	0	7,405
Hedging reserve	651	0	651
Translation reserve	(37,880)	0	(37,880)
Accumulated deficit	(277,237)	0	(277,237)
Total equity	**463,155**	**232,079**	**695,234**
Total Capitalisation	512,769	0	814,524
Cash and cash equivalents	121,591	301,755	423,346
Total current debt	17,446	0	17,446
Net current Financial debt	(104,145)	(301,755)	(405,900)
Total non current debt	32,168	0	32,168
Net Financial debt	(71,977)	(301,755)	(373,732)

(1) The amounts of secured current and non-current debt as at June 30, 2009 refer to the financial lease obligations and mortgage loan. We present these as financial liabilities in our consolidated financial statements.

As of 30 June 2009, our authorized capital amounted to € 75,000,000 and was divided into 156,250,000 Shares and 156,250,000 preference shares, all with a nominal value of € 0.24 each.

As of 30 June 2009, 66,561,032 Shares were outstanding and were fully paid up.

Except for the proceeds of the New Shares received on 28 September 2009 which have been incorporated in the table above and other than due to our ordinary course of business (such as seasonality) and the financing of our new production facility in South Korea, there has been no material change to our consolidated cash and cash equivalents, capitalization and indebtedness since 30 June 2009.

7 SELECTED FINANCIAL DATA

The tables below set forth our selected consolidated financial data as at the dates and for the periods indicated. The selected consolidated financial data should be read in conjunction with the remainder of this Prospectus including (i) the Audited Financial Statements incorporated by reference into this Prospectus, (ii) the Semi-Annual Financial Statements incorporated by reference into this Prospectus, and (iii) Chapter 8 "Operating and Financial Review" in this Prospectus.

Our Audited Financial Statements incorporated by reference herein have been prepared in accordance with IFRS and have been audited by Deloitte Accountants B.V., independent auditors. The selected consolidated financial data set forth below is extracted without material adjustment from our Audited Financial Statements and our Semi-Annual Financial Statements. The selected consolidated financial data set forth below may not contain all of the information that is important to prospective investors.

In thousands of euro	**Year Ended 31 December**			**6 months period ended June 30**	
	Audited			**Unaudited**	
	2008	**2007**	**2006**	**2009**	**2008**
Product sales	226,055	177,569	103,918	129,566	83,910
License revenues	30,202	12,211	16,955	7,978	10,755
Service fees	10,900	14,006	10,694	5,362	4,302
Total revenues	**267,157**	**203,786**	**131,567**	**142,906**	**98,967**
Cost of product sales	(138,790)	(124,557)	(83,518)	(78,393)	(58,760)
Cost of service and license fees	(6,965)	(10,327)	(6,971)	(4,893)	(2,603)
Total cost of goods sold	**(145,755)**	**(134,884)**	**(90,489)**	**(83,286)**	**(61,363)**
Gross margin	**121,402**	**68,902**	**41,078**	**59,620**	**37,604**
Government grants	5,380	7,086	6,901	2,027	2,103
Other income	10,772	2,244	2,455	7,480	6,458
Total other operating income	**16,152**	**9,330**	**9,356**	**9,507**	**8,561**
Research and development	(70,229)	(63,995)	(67,606)	(31,239)	(33,455)
Selling, general and administrative	(64,350)	(61,752)	(46,732)	(32,337)	(29,956)
Restructuring	-	-	(3,120)	-	5,153
Reversal of impairment / (impairment)	4,888	(171)	(30,416)	-	_
Total other operating expenses	**(129,691)**	**(125,918)**	**(147,874)**	**(63,576)**	**(58,258)**
Operating profit (loss)	**7,863**	**(47,686)**	**(97,440)**	**5,551**	**(12,093)**
Financial income and expense	(2,662)	1,378	1,747	(2,843)	(2,093)
Result investments non-consolidated companies	(128)	(996)	(1,956)	225	(183)
Result disposal of non-consolidated companies	1,570	2,186	-	-	-
Disposal of subsidiaries	(367)	-	-	-	-
Profit (loss) before tax	**6,276**	**(45,118)**	**(97,649)**	**2,933**	**(14,369)**
Income tax	8,310	2,208	10,451	(4,573)	(1,515)
Profit / (loss) for the year	**14,586**	**(42,910)**	**(87,198)**	**(1,640)**	**(15,884)**
Attributable to:					
Equity holders of the parent	14,586	(42,910)	(86,946)	(1,640)	(15,884)
Minority interest	-	-	(252)	-	-
Weighted average shares outstanding - basic	65,593	65,103	57,064	66,338	65,478
Weighted average shares outstanding - diluted	66,315	65,103	57,064	67,934	65,478

In thousands of euro	Year Ended 31 December			6 months period ended June 30	
	Audited			Unaudited	
	2008	2007	2006	2009	2008
Selected data from statements of financial position					
Cash and cash equivalents	170,969	163,248	157,837	121,591	106,883
Current assets excluding cash	151,349	140,014	159,234	192,686	156,066
Current liabilities	118,301	114,742	90,252	110,285	88,520
Shareholders' equity	453,492	441,103	497,886	463,155	413,322
Selected cash flow data					
Cash flows (used) from operating activities	(254)	22,194	(53,954)	(26,945)	(51,944)
Cash flows from (used) in investing activities	(8,907)	(24,241)	23,159	(17,491)	(52)
Cash flows from (used) in financing activities	16,626	11,244	78,371	(4,751)	(4,070)

8 OPERATING AND FINANCIAL REVIEW

You should read the following in conjunction with Chapter 7 "Selected Financial Data" and our Audited Financial Statements and Semi-Annual Financial Statements that are incorporated by reference in this Prospectus. Our consolidated financial statements incorporated by reference herein have been prepared in accordance with IFRS. Our unaudited consolidated interim financial statements incorporated by reference herein have been prepared in accordance with IAS 34 'Interim Financial Reporting'.

In addition to historical information, the following review includes forward-looking information that involves risks, uncertainties and assumptions. Our actual results and the timing of events could differ materially from those anticipated by these forward-looking statements as a result of many factors, including those discussed below and elsewhere in this Prospectus, particularly under Chapters 2 "Risk Factors" and 3.5 "Important Information - Forward-looking statements".

8.1 Overview

Crucell is a fully integrated biopharmaceutical company. We focus on developing, producing and marketing products that combat infectious diseases. We are the largest independent vaccine company in the world. Headquartered in Leiden, the Netherlands, Crucell currently employs about 1,100 people and has subsidiaries in Switzerland, Spain, Sweden, Italy, South Korea, the United Kingdom and the United States. Our vaccine business provides stable and predictable sales and cash flow. We have sold more than 100 million vaccine doses in over 80 countries throughout the world, which makes us the largest independent vaccine player. Within vaccines we operate in three main markets: paediatric, travel and endemic, and respiratory.

In thousands of euro	**Year ended 31 December**			**% - Change**	
	2008	**2007**	**2006**	**08 vs. 07**	**07 vs. 06**
Paediatric vaccines	111,039	77,371	35,933	43.5	115.3
Respiratory vaccines	32,474	33,188	40,386	(2.2)	(17.8)
Travel and endemic vaccines	55,572	47,282	23,072	17.5	104.9
Other products	26,970	19,728	4,527	36.7	335.8
Total product sales	**226,055**	**177,569**	**103,918**	**27.3**	**70.9**

In thousands of euro	**Year ended 31 December**			**% - Change**	
	2008	**2007**	**2006**	**08 vs. 07**	**07 vs. 06**
Product sales	226,055	177,569	103,918	27.3	70.9
License revenues	30,202	12,211	16,955	147.3	(28.0)
Service fees	10,900	14,006	10,694	(22.2)	31.0
Total revenues	**267,157**	**203,786**	**131,567**	**31.1**	**54.9**

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 locations of the customers.

In thousands of euro	Year ended 31 December		
	2008	2007	2006
Europe	209,473	144,969	94,663
North America	33,653	33,346	13,868
Asia	19,095	18,589	16,506
Other	4,936	6,882	6,530
Total	**267,157**	**203,786**	**131,567**

8.2 Material factors affecting our results of operations and financial condition

The main material factors affecting our results of operations and financial condition are:

- foreign currency risks;
- profitability and sales of products due to tax law changes;
- weakness in the global economy.

For further details about these factors we refer to Chapter 2 "Risk Factors".

8.3 Recent developments

On August 17, 2009 the Company announced that a large supranational organization has awarded the first portion of new contracts worth $ 300 million for supplies of Crucell's Quinvaxem paediatric vaccine. The new contracts are the largest ever received by Crucell and cover the period 2010-2012, with the initial awarded amount expected to grow even further over those three years

On August 18, 2009 the Company announced that it received a contract from National Institute of Allergy and Infectious Diseases (**NIAID**)/National Institutes of Health (**US NIH**) aimed at advancing the development of monoclonal antibodies for the treatment of seasonal and pandemic influenza. The contract provides funding of up to $ 40.7 million, with additional options that may be triggered at the discretion of the US NIH worth a further $ 28.4 million, bringing the potential total amount to $ 69.1 million.

8.4 Revenues

Total revenues and other operating income amounted to € 152.4 million for the first half of 2009, an increase of 42% compared to the same period in 2008. The increase was mainly driven by growth in sales of our paediatric vaccines, in particular Quinvaxem®.

In 2008, total revenues increased by € 63.4 million or 31.1% from € 203.8 million in 2007 to € 267.2 million in 2008. The increase is attributable to an increase in product sales of € 48.5 million or 27.3% and license revenues of € 18.0 million or 147.3%. The increase is partly offset by a decrease in revenue from service fees of € 3.1 million or (22.2%).

In 2007, total revenues grew by € 72.2 million or 54.9% from € 131.6 million in 2006 to € 203.8 million in 2007. The increase is primarily attributable to increases in sales of paediatric vaccines by € 41.4 million or 115.3% and travel and endemic vaccines by € 24.2 million or 104.9% and higher revenues relating to the acquisitions made in the second half of 2006.

In 2006, total revenues increased to € 131.6 million from € 32.7 million in 2005, an increase of 302%. The increase in total revenues was mainly attributable to product sales following the acquisitions of Berna Biotech AG in February 2006 and SBL Vaccin AB in November 2006.

Product sales

Product sales in the first half of 2009 amounted to € 129.6 million and represent sales of paediatric vaccines (66%), travel and endemic vaccines (22%), and other products (12%).

In 2008, product sales grew by € 48.5 million or 27.3%. The increase is primarily attributable to increased sales of paediatric vaccines of € 33.7 million or 43.5%, travel and endemic vaccines of € 8.3 million or 17.5%, and other products of € 7.3 million or 36.7%.

In 2008, paediatric vaccines grew mainly as a result to increased Quinvaxem sales. Supranational organizations awarded us additional contracts for Quinvaxem and Hepavax Gene amounting to $ 140 million for the period 2008-2009. Travel and endemic vaccines showed considerable growth on an overall basis. 'Other products' include sales of vaccine and proteins trade goods that we distribute for third parties and also sales of conjugates to Wyeth. The increase in other products 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.

Our core product portfolio consists of seven vaccines: Quinvaxem, Hepavax-Gene, MoRu-Viraten (paediatric vaccines), Inflexal V (respiratory), Dukoral, Epaxal and Vivotif (travel and endemic vaccines). The aggregated revenues for our core product portfolio amounted to € 191.6 million in 2008 (2007: € 151.8 million, 2006: € 92.1 million) and represented 84.8% (2007: 85.5%, 2006: 88.6%) of our total product sales.

In 2008, sales to our two largest customers who are in the paediatric vaccines area amounted to € 85.1 million or 37.6% and € 18.4 million or 8.1% of net product sales. In 2007, sales to these customers accounted for € 45.5 million or 25.6% and € 23.5 million or 13.2% of net product sales, respectively.

In 2007, product sales grew by € 73.7 million or 70.9%. The growth in revenue from product sales was mainly due to increased revenue from sales of paediatric vaccines of € 41.4 million or 115.3%, travel and endemic vaccines of € 24.2 million or 104.9%, and sales of other products of € 15.2 million or 335.8%. The increase in product sales was partly offset by a decrease in respiratory vaccines of € 7.2 million, mainly caused by lower influenza vaccine sales as a result of a mild flu-season in 2007.

The majority of our sales are export sales. Domestic product sales amount to € 3.7 million or 1.6% (2007: € 0.7 million or 0.4% and 2006: nil). Almost all of our license revenues and service fees are billed to foreign parties.

In 2006, product sales amounted to € 103.9 million. The increase is solely due to the companies acquired in 2006. We had no product sales in the previous year.

License revenues

License revenues were € 8.0 million in the first half of 2009, a decrease of € 2.8 million compared to the same period in 2008, which included milestone payments.

In 2008, license revenues increased by € 18.0 million or 147.3% to € 30.2 million compared to 2007. This increase mainly resulted from milestone payments relating to the rabies and influenza programs from Sanofi Pasteur and upfront fees received from Talecris for the exclusive production rights of two specific proteins.

In 2007, our license revenues decreased to € 12.2 million, a reduction of € 4.7 million or 28.0% compared to 2006, which was mainly due to one-off issuance fees included in contracts with DSM and Sanofi Pasteur in 2006. The underlying agreements with DSM and Sanofi Pasteur are still in effect. The decrease was partly offset by recognized issuance fees on contracts signed in 2007 with MedImmune, ADImmune and Wyeth that totalled € 4.3 million and numerous other, smaller, contracts.

In December 2007, we signed an exclusive collaboration and commercialization agreement with Sanofi Pasteur relating to our rabies monoclonal antibodies. We received a payment of € 10.0 million, which will be recognized as license revenues over the period that the development activities are performed. We will be eligible for additional potential milestone payments of up to € 66.5 million.

In 2006, license revenues decreased by € 3.9 million to a total of € 17.0 million compared to 2005. The decrease is mainly caused by developments under the following contracts. Total license revenues generated on IAVI (International AIDS Vaccine Initiative) contracts decreased by € 2.6 million; license revenues on DSM contracts decreased by € 1.4 million; license revenues on sanofi contracts decreased by € 1 million. This reduction was partially offset by several contracts with other parties such as Merck and Ferring.

Service fees

Service fees for half year 2009 were € 5.4 million, compared to € 4.3 million last year. Service fees represent revenues for product development activities performed under contract with partners and licensees.

In 2008, service fees amounted to € 10.9 million, a decrease of € 3.1 million or 22.2% compared to 2007. In 2008, service fees on the Sanofi Pasteur influenza project were lower compared to 2007. Service fees include revenues relating to various collaboration agreements. Typically we do not retain a residual interest in products developed under these agreements. We are more selective in the programs that we want to carry out and we tend to put more focus on the profitability of these types of programs.

In 2007, service fees amounted to € 14.0 million, an increase of € 3.3 million or 31.0% compared to 2006. This increase was mainly attributable to consulting services provided to ADImmune and to increased service fees in Sweden realized on miscellaneous projects.

In 2006, service fees amounted to € 10.7 million, a decrease of € 1.2 million or 10% compared to 2005. This decrease was mainly due to lower service fees generated on contracts related to the NIAID.

Other Operating income

Government grants

In 2008, government grants decreased by € 1.7 million 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.

In 2007, government grants were stable compared to 2006. The most significant grants in 2007 were received from NIAID for further research on HIV and from SenterNovem. The increase in 2006 compared to 2005 was mainly the result of additional subsidies from NIAID for further research on HIV.

Other income

Other income mainly consists of the reimbursement of development costs and funding received from non-governmental agencies. Other income also includes non-core business transactions such as the sale of property, plant and equipment and income generated from training courses.

In 2008 other income increased by € 8.5 million 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.

The amount of other income in 2007 was stable compared to 2006. The increase in 2006 compared to 2005 is due to the other income generated in the companies that were acquired in 2006.

8.5 Operating costs

Cost of goods sold

The cost of goods sold comprises direct labour, materials, and overhead costs incurred in performing work under various collaboration agreements directly relating to product sales.

The cost of goods sold for the first half of 2009 amounted to € 83.3 million, € 78.4 million of which represents product costs and € 4.9 million the cost of service and license activities. Gross margins were 42% in the first half year of 2009, compared to 38% in the same period of 2008. Although our margins improved significantly in comparison with last year, this effect was negatively influenced by a stronger Swiss Franc against the euro and Korean Won against the US dollar, which increased our reported costs of goods sold on a consolidated basis. We expect continued pressure on margins in the second half of the year as a result of exchange rates.

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 included additional expenses of € 3.5 million (2007: € 10.2 million) relating to the purchase price allocations of the businesses acquired by the Group. The gross margin on product sales amounted to 38.6% (2007: 29.9%). The percentage increase in gross margin was 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 in purchase price allocation charges in 2008.

The cost of product sales increased in 2007 mainly due to the increase in product sales of 70.9%. This increase was partly offset by the reduction in purchase price allocation charges in 2007. The 2007 cost of product sales included additional expenses of € 10.2 million (2006: € 16.2 million) relating to the purchase price allocations of the acquired businesses. The gross margin on product sales amounted to 29.9% (2006: 19.6%). The percentage increase in gross margin was mainly due to a reduction in purchase price allocation charges in 2007.

The cost of product sales amounted to € 83.5 million in 2006. The company had no product sales in the previous year.

Cost of service fees

The cost of service fees comprised direct labour, materials and overhead costs relating to work under various collaboration agreements. We do not retain a residual interest in products developed under the agreements and will not normally have ownership of intellectual property rights in these products.

In the first half of 2009 the cost of services fees increased to € 4.9 million, compared to € 2.6 million in the same period in 2008. This increase was due to increased levels of activity.

In 2008, the cost of service fees decreased by € 3.4 million 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. In 2008, there was a shift in strategy to focus more on programs that generate higher margins.

In 2007, the cost of service fees increased by € 3.4 million or 48.1% compared to 2006, which is primarily attributable to an increase in service fee revenues by 31.0%. The gross margin on service fees was 26.3% in 2007 compared to 34.8% in 2006.

In 2006 the cost of service fees decreased by € 0.2 million or 2.6% compared to 2005. The decrease reflected the lower level of services fee revenues, which reduced the expenses. The gross margin on service fees was 34.8% in 2006 compared to 39.8% in 2005.

Other operating expenses

Research and development expenses

R&D 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 relating to R&D, and lease expenses for lab space and equipment lease. R&D expenses also include fees we pay to third parties who conduct research on our behalf.

R&D expenses for the first half of 2009 amounted to € 31.2 million, which represents a € 2.2 million decrease as against the first half of 2008.

R&D expenses increased in 2008 by € 6.2 million or 9.7% compared to 2007. This increase was mainly attributable to increased expenditures on the rabies programme for which two phase II clinical trials were performed.

R&D expenses comprised 54.2% of total other operating expenses in 2008 (2007: 50.8%). We expect that R&D expenses will continue to be a significant portion of our overall expenses in the future.

In 2007, R&D expenses decreased by € 3.6 million or 5.3% compared to 2006, which was primarily attributable to the cost-saving effect of the restructuring programme that took place in 2006 to centralize R&D activity in Leiden and to phasing out work on both a vaccine candidate as well as on programs at the Centre of Mammalian Cell Culture.

In 2006 research and development expenses increased by € 33.6 million or 98.6% compared to 2005. An amount of € 27.3 million of this increase can be attributed to the research and development programs of the companies that were acquired in 2006. The remaining increase of € 6.2 million is the result of the increased number of development programs progressing into the clinical phase.

Selling, general and administrative expenses

Selling, general and administrative expenses consist of personnel expenses and other operating expenses in marketing and sales, finance, human resources, investor relations, and legal and general management.

The expenses for the first half of 2009 were € 32.3 million, which represents a € 2.4 million increase when compared with the first half of 2008.

These expenses increased in 2008 by € 2.6 million or 4.2% to € 64.4 million compared to € 61.8 million in 2007. This increase was primarily due to the overall growth of the Group as a whole. Specific items were 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 was partly offset by cost reductions realized through our Healthy Ambition programme.

Selling, general and administrative expenses increased in 2007 by € 15.0 million or 32.1% to € 61.7 million, compared to € 46.7 million in 2006. Selling costs increased as a result of the cost base of the companies acquired in 2006, which were included for a whole year for the first time in 2007. General and administrative expenses also included integration costs of the acquisitions in 2006 and additional costs relating to compliance with internal control over financial reporting requirements under US law.

In 2006 selling, general and administrative expenses amounted to € 46.7 million, compared to € 13.7 million in 2005. Selling costs increased as a result of the cost base of the companies acquired in 2006. General and administrative expenses also included integration costs of the 2006 acquisitions and additional costs relating to compliance with the internal control over financial reporting requirements under U.S. law.

Restructuring

A restructuring programme in our Italian subsidiary Berna Biotech Italia Srl. was executed in 2008. A total provision of € 0.7 million was recognized, of which € 0.6 million was recorded in restructuring provisions at year-end 2008. The majority of this provision was paid in the first quarter of 2009. The costs for the restructuring were included in the applicable operating expenses as they were of operating nature.

There were no restructuring expenses in 2007.

The restructuring expenses in 2006 were related to centralizing R&D functions in Leiden and to phasing out R&D projects in Switzerland, including the candidate vaccine Aerugen, and the Centre of Mammalian Cell Culture. The decision to concentrate R&D in Leiden was made to increase efficiency in R&D spending. The provision was recognized in 2006 as recognition criteria were met at that time. The actual reduction in the number of staff employed was effected in the first quarter of 2007.

Impairment

In the first quarter of 2008, we reversed € 5.2 million of previously impaired property, plant and equipment. In 2008, we entered into an exclusive agreement with Wyeth Pharmaceuticals in which we will develop and manufacture 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, as described below. 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 € 0.3 million for the animal housing facility in Bern, Switzerland that was no longer in use. As there was no alternative use for this building for any of the Group's other activities and the building could not be sold directly to other parties as it was on our campus, the Group impaired the carrying value to zero.

In 2007, we recognized an impairment charge of € 0.2 million for a warehouse in South Korea that was demolished to make way for the construction of a light railway.

In 2006, we recognized a total impairment of € 30.4 million. The impairment related to two buildings in Switzerland, including installed equipment, for an amount of € 19.6 million, and to acquired in-process R&D relating to the Tetra vaccine for an amount of € 10.8 million.

8.6 Financial income and expense

Financial income and expenses mainly consist of interest income and expenses, foreign exchange losses and other financial expenses.

Net financial expenses in the first half of 2009 were € 2.8 million. This was a result of lower interest income offset by negative currency effects on our balance sheet (net working capital) positions.

In 2008, the negative result on net financial income and expenses totalled € 2.6 million and consisted of interest income of € 5.0 million, foreign exchange losses of € 3.9 million, interest expenses of € 2.7 million, and other financial expenses of € 1.0 million.

Net financial income and expenses decreased by € 4.0 million or 293.2% compared to 2007. The decrease was primarily attributable to foreign exchange losses of € 3.9 million. 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 subsidiary Berna Biotech AG. In addition, foreign exchange losses were realized on euro liabilities and on losses on US dollar transactions in South Korea. Other changes in net financial income and expenses were:

- A reduction in interest income € 0.7 million, mainly caused by a lower average cash balance in 2008 compared to 2007;
- Increased interest expenses of € 0.4 million as a result of increased finance leases and short-term financial liabilities; and
- An increase in other financial expenses of € 0.3 million primarily due to factoring arrangements engaged in during 2008.

In 2007, net financial income and expenses decreased by € 0.4 million or 21.1% compared to 2006. The decrease was primarily attributable to:

- Increased negative foreign exchange results of € 1.1 million as the foreign currencies in which we traded lost value compared to the euro;
- Increased interest expenses of € 0.5 million as a result of additional charges relating to leasing and to the full year effect of our 2006 acquisitions; and
- An increase in other financial expenses of € 0.4 million primarily due to factoring arrangements entered into during 2007. The decrease was partly offset by increased interest income of € 2.0 million resulting primarily from higher interest rates in 2007.

In 2006, net financial income and expenses amounted to € 1.7 million and mainly consisted of interest income of € 3.7 million on cash balances and interest expenses of € 1.8 million. The interest expenses related to the mortgage loan in the Netherlands that was used to finance the new production facility and the loan obligations of the companies acquired in 2006.

8.7 Liquidity and capital resources

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 € 121.6 million, € 171.0 million, € 163.2 million and € 157.8 million as of 30 June 2009, 31 December 2008, 31 December 2007 and 31 December 2006, respectively.

Borrowing requirements are limited and primarily relate to mortgage funding. For further details on our existing financing facilities, please refer to Chapter 8.9 "Operating and Financial Review – Contractual obligations" .

8.8 Cash flows

Net cash flows from/(used in) operating activities

Cash and cash equivalents decreased by € 49.4 million in the first half of 2009 to € 121.6 million. Cash used for operating activities in the half year, including working capital, amounted to € 26.9 million. This reflects the seasonality of our business, in which we build inventory in the first half of the year to sell our products in the second half of the year.

In 2008, our net cash flow from operating activities decreased by € 22.4 million or 101.1% compared to 2007. The decrease resulted from an increase in our working capital of € 54.6 million and a reduction in the adjustments for non-cash items by € 25.8 million. The decrease was partly offset by € 57.5 million 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 € 54.5 million. 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 € 30.9 million due to build-up of Quinvaxem inventory for 2009 sales, and other current liabilities for € 22.3 million.

In 2008, adjustments for non-cash items were reduced by € 25.8 million. This reduction was mainly caused by:

- One-off cash receipts in 2007 in the amount of € 11.5 million 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 € 4.7 million 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 € 5.2 million as we now perform contract manufacturing at this location.

In 2007 our net cash flow from operating activities increased by € 76.1 million or 141.1% compared to 2006. The increase resulted from a reduction in our net loss of € 44.3 million and a reduction of our working capital of € 47.3 million. The increase is partly offset by a decrease in the adjustments for non-cash items by € 13.9 million and an increase in interest and taxes paid by € 1.6 million in 2007.

In 2006 the net cash flows used in operating activities increased by € 38.9 million or 259.5% compared to 2005. This is mainly due to the increase of the operations resulting from the companies acquired in 2006.

Net cash flows from/(used in) investing activities

In the first half of 2009 we used € 17.5 million cash for investing activities, reflecting the capital investment in our new plant in South Korea. We intend to invest up to € 25 million (including € 17.5 million) of our own funds in the facility in 2009 and 2010.

Our cash flow used in investing activities amounted to € 8.9 million in 2008, compared to € 24.2 million 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 € 15.8 million. These investments mainly related to our new South 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 € 4.4 million in 2008 (2007: € 5.3 million);
- The sale of all shares owned by the Group in Kenta Biotech AG for € 1.5 million to Ingro Finanz AG; and
- Restricted deposits that were transferred to cash and cash equivalents for € 1.5 million.

In 2007, the most significant cash flows used in investing activities were from the following transactions:

- Investments made in property, plant and equipment for an amount of € 27.2 million in 2007. The investments in 2007 mainly related to our new GMP production facility in Leiden, the Netherlands and investments in our facilities in Bern, Switzerland which will improve current production processes and allow in-house production of materials currently acquired from third parties.
- The Company acquired a 20% equity stake in Taiwan-based ADImmune Corp. in March 2007 for € 8.9 million.

In 2007, the most significant cash flows from investing activities were from the following transactions:

- The sale of all shares owned by the Company in Pevion Biotech AG, Switzerland for € 6.1 million to other shareholders of Pevion Biotech, and
- Interest received of € 5.3 million in 2007 (2006: € 3.1 million).

In 2006 the net cash flows from investing activities amounted to € 23.2 million. The most significant transactions leading to a cash in-flow from investing activities were the following:

- The acquisition of Berna Biotech AG resulted in a net cash in-flow of € 67.8 million. Although the acquisition itself was completed by a share exchange and the cash used for acquisition costs amounted to € 10.1 million, we acquired € 77.9 million cash in the acquisition;
- The sale of Berna Biotech AG's veterinary division, which included Dr. E. Graub AG and Berna Veterinary AG and the divestment of the biopharmaceutical and vaccine manufacturer Rhein Biotech caused a cash in-flow of € 11.8 million;
- The reduction of restricted cash at Berna Biotech AG accounted for a net cash inflow of € 7.6 million; and
- Interest received of € 3.1 million in 2006.

The cash in-flow is partly offset by the following transactions:

- The acquisition of SBL Vaccin AB caused a net cash-outflow of € 33.4 million. The acquisition price, including acquisition costs, amounted to € 40.5 million. Crucell acquired € 7.1 million cash in the acquisition;

- Investments made in property, plant and equipment for an amount of € 20.4 million in 2006. Investments were mainly related to building and equipping our new GMP production facility in Leiden, the Netherlands; and

- Acquisitions of intangible assets in 2006 for € 12.4 million related to the acquisition of the assets and liabilities of Berna Products Corp.

Net cash flows from / (used in) financing activities

In the fist half of 2009 our cash used for financing activities amounted to € 4.8 million, reflecting partial repayment of our loan in South Korea, offset by proceeds from the issue of shares relating to stock option exercises.

Our cash flow from financing activities amounted to € 16.6 million in 2008, € 11.2 million in 2007 and € 78.7 million in 2006.

In 2008, the cash flow from financing activities increased by € 5.4 million or 47.9% compared to 2007 and mainly related to:

- Additional short-term financing facilities in South Korea for an amount of € 22.2 million; and

- Finance leases with proceeds of € 12.4 million 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 South Korea for € 11.9 million and a partial redemption of a short-term euro loan also in South Korea for € 1.5 million;

- Settlement of financial liabilities relating to factored Italian trade accounts receivables for € 5.7 million 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 € 1.9 million.

In 2007, the cash flow from financing activities decreased by 67.5 million or 85.7% compared to 2006 as we limited the use of additional financing and funded our operations and investments with own resources. The cash-flow inflow from financing activities in 2007 mainly related to:

- Factoring of trade accounts receivables in Italy for an amount of € 5.7 million, and

- Finance leases with proceeds of € 4.2 million. These finance leases mainly related to equipment for the new production and development facility in Leiden.

In 2006 the Company had a cash in-flow from financing activities of € 78.7 million that mainly related to the following:

- Proceeds of € 76.8 million from the private placement of ordinary shares in November 2006;

- Proceeds from the issuance of ordinary shares in relation to the exercise of employee stock options of € 6.0 million;

- The Company drew € 8.1 million under the terms of the mortgage loan for financing the new GMP production facility in Leiden, Netherlands; and

- The Company entered into new finance lease contracts in 2006 with proceeds of € 6.5 million. These finance leases mainly relate to equipment for the new production and development facility in Leiden.

The increase was partly offset by repayments of financial liabilities on the balance sheet of Berna Biotech for an amount of € 17.8 million.

Working capital statement

Our current cash resources, together with our existing financing facilities, do provide us with sufficient working capital for at least the next 12 months following the date of this Prospectus. This working capital statement covers us and all our current subsidiaries.

For further details on our existing financing facilities, please refer to Chapter 8.9 "Operating and Financial Review – Contractual obligations".

8.9 Contractual obligations

Financial lease obligations

It is our policy to lease our equipment in order to reduce the substantial cash outlay associated with investments in these. This has resulted in total finance lease obligations of € 20.5 million as of 31 December 2008, € 10.1 million as of 31 December 2007 and € 7.0 million as of 31 December 2006. 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 to 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 31 December 2008 and 2007 are as follows:

In thousands of euro	**2008**		**2007**	
	Minimum payments	**Present value of minimum payments**	**Minimum payments**	**Present value of minimum payments**
Within one year	4,134	2,777	2,038	1,420
After one year but not more than five years	17,284	14,292	10,937	8,660
More than five years	3,580	3,457	-	-
	24,998	**20,526**	**12,975**	**10,080**

Mortgage loan Netherlands

In December 2005, the Group entered into a euro mortgage loan of up to € 17.1 million and as of 31 December 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 1 January 2007, the loan is being repaid through monthly payments over 15 years. A balloon repayment of € 10.0 million will be made at the end of the 15 years. The loan matures on 31 December 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 € 10.0 million secure the loan. The carrying amount of the underlying secured assets was year-end 2008 € 24.0 million (2007: € 26.9 million).

Mortgage loan Korea

On 26 March 2009 we entered into a mortgage loan facility in South Korea for an amount of KRW 50 billion (€ 27.7 million) to partly finance the investments in the new South Korean facility in 2009. 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 June 30, 2009, no funds were drawn from the mortgage facility. In August 2009 we have drawn (an initial) KRW 5 billion under the facility. Crucell NV provided the third party bank with a guaranty amounting to KRW 50 billion plus interest and other costs.

Comprehensive credit limit Berna Biotech Korea Corp.

On 12 June 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 31 May 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 South Korean interest index plus a mark-up. At 31 December 2008 the interest percentage was 6.79% and an amount of KRW 37 billion (€ 20.9 million) was drawn under the agreement. In 2009 the period was extended to 31 May 2010 and an amount of KRW 25 billion (€ 13.9 million) has been drawn as at 30 June 2009.

Loan Berna Biotech Korea Corp.

Berna Biotech Korea Corp. had an unsecured euro loan that bears interest at 5.45% which was outstanding at 31 December 2008. The original maturity date of the loan was 1 August 2010, but the loan was repaid in full on 2 February 2009.

Privately placed bond Berna Biotech Korea Corp.

Berna Biotech Korea Corp. issued a Korean Won-denominated bond with an interest rate of 6.73%. The privately placed bond by Berna Biotech Korea Corp. was repaid on 13 June 2008.

Factoring liabilities

In December 2007, the Group factored trade accounts receivables for a total amount of € 5.7 million with an external party in Italy. The Group did not transfer substantially all the risks and rewards associated with ownership of the transferred trade accounts receivables, specifically the credit risk, and consequently the cash payments received are accounted for as a financial liability. No interest is charged on the factoring liabilities.

8.10 Statement of significant change

There has been no significant change in the trading or financial position of the Group since 30 June 2009, the date to which our most recent unaudited condensed consolidated interim financial statements were prepared. However, please note that our operations and sales are primarily denominated in foreign currencies and as a result currency movements may impact our results significantly. We refer to Chapter 2 “Risk Factors”.

8.11 Off-balance sheet arrangements

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 31 December 2008, 2007 and 2006 are as follows:

In thousands of euro	Year ended 31 December		
	2008	2007	2006
Within one year	3,830	4,798	5,794
After one year but not more than five years	10,073	15,308	14,680
More than five years	10,759	14,155	16,658
	24,662	**34,261**	**37,132**

Most operating leases are increased by a general price index on an annual basis.

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 into 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. The expense was recognized in the cost of goods sold. No payments were made in 2008.

Unconsolidated companies

As of 31 December 2008, 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 (ADImmune Corp.) and in one joint venture (Percivia LLC) that are classed as non-consolidated companies in accordance with IFRS.

In the first half of 2009, there were no material changes to the Group's commitments or contingent liabilities from those disclosed in the 2008 Financial Statements other than 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 provided Novartis with collateral on our Swiss premises. This amount was increased to CHF 45.0 million (€ 29.5 million) compared to CHF 34.0 million at year-end 2008.

8.12 Critical accounting policies and estimates

Our discussion and analysis of our financial position and results of operations are based on our consolidated financial statements, which have been prepared in accordance with IFRS. The preparation of these financial statements requires us to make estimates and judgements that affect the reported amounts of assets, liabilities, revenues and expenses and related disclosure of contingent assets and liabilities. On an ongoing basis, we evaluate our estimates based on historical experience and make various assumptions that we believe to be reasonable under the circumstances, the results of which form the basis for making judgments about the carrying values of assets and liabilities that are not readily apparent from other sources. Actual results may differ from these estimates under different assumptions or conditions. A summary of our significant accounting policies is contained in our consolidated financial statements, which are incorporated by reference in this Prospectus. We consider the following estimates and judgements to be critical to the understanding of the results of our operations.

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 that may only be recognized if they are 'substantive'. Determining whether a milestone is substantive also requires management judgment.

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 (substantially) 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 our tax returns by tax authorities, the Group may need to adjust the valuation of our 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, 2008, the Group had unrecognized tax carry forward losses of € 172.7 million (2007: € 254.5 million, 2006: € 222.3 million) that are available, with certain restrictions in time, for offset against future taxable profits of the companies in which the losses arose.

Management assessed the likelihood that the carry forward losses will be recovered from future taxable profit. To the extent Management believes that recovery is probable, a deferred tax asset was recognized, which at December 31, 2008 was € 9.0 million (2007: € 0.7 million, 2006: € 0.7 million). To the extent the likelihood of recovery of deferred tax assets changes, an expense or a gain within the tax charge in our income statement for the relevant period will be included.

Accounting for 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) of the acquired business at the estimated fair values at acquisition date. Judgments, made in identifying and valuating assets and liabilities assumed in a business combination and in determining the useful life of any acquired assets, can significantly affect both current period as future periods operating results. Estimated fair values in a business combination are based on information available at the date that the purchase price allocation is completed. Assets and liabilities may be adjusted or recognized retrospectively within the period of one year if management receives additional information about facts and circumstances that existed at the acquisition date.

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 that were identified in a business combination, but not valued separately because the assets were either not separable or could not be measured reliably. Assets identified and included as part of goodwill can be specific customer relationships, supply contracts not meeting the recognition requirements or the workforce acquired. Goodwill recognized can significantly affect both current period as future periods operating results as goodwill is subject to an annual impairment review and not to periodical amortization.

Goodwill at December 31, 2008 amounted to € 46.0 million compared to € 44.4 million at the end of 2007. Goodwill increased due to a strengthening of the foreign currencies underlying the investment in the foreign operations. The increase is mainly caused by the appreciation of the Swiss franc and the US dollar against the euro in 2008.

Impairment reviews of property, plant and equipment, intangible assets and goodwill

An asset's recoverable amount is the higher of the asset's fair value less costs to sell and its value in use. For goodwill, the recoverable amount is tested at the level of the cash generating unit. The Group starts its impairment reviews of property, plant and equipment, intangible assets and goodwill by determining the asset's (or cash generating unit'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 asset is impaired. The best evidence of an asset'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 asset. However for most of the Group's assets there are typically no observable market prices as the assets have a level of specificity for which no active market exists. The fair values less costs to sell are predominantly based on discounted net present value calculations that use assumptions applicable in the current market. Key assumptions are those regarding the discount rates, the estimated terminal growth rate, expected changes to market share and the selling prices and costs in the forecasted period. Where applicable, the forecasted cash flows for pre-clinical programs are adjusted for the risk of failure of the program.

Property, plant and equipment and intangible assets

The Group assesses for its property, plant and equipment and intangible assets at each reporting date whether there is an indication that an asset may be impaired. If there is such an indication of impairment or when an annual impairment test for an asset is required, an impairment test is performed.

In the year ended December 31, 2006, an impairment loss of € 19.6 million was recognized for two buildings, including installed equipment, that were acquired in the business combination with Berna Biotech AG. Both buildings are located in Switzerland. Berna Biotech 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. The buildings are specially configured for biotechnology purposes and it is impracticable to separate the equipment from the buildings. Since at the time there was no direct use for these buildings for any of the Group's other activities, no market for the sale of the buildings to third parties and no expectation that these buildings could be utilized in the foreseeable future, an impairment was recorded for the total carrying amount of € 19.6 million as at December 31, 2006.

In the fourth quarter of 2006 an impairment loss of € 10.8 million was recognized on the in-process research and development of the Tetra vaccine which was acquired in February 2006 when the Company acquired Berna Biotech AG. Management decided to stop the development of Tetra after Quinvaxem received approval by the WHO. Consequently, the carrying value of Tetra was impaired for the total amount of € 10.8 million.

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. In the first quarter of 2008, the Group entered into an exclusive agreement with Wyeth Pharmaceuticals. The Group develops and manufactures certain components of a vaccine for use by Wyeth in clinical studies. The contract manufacturing takes place in one of the two buildings that was impaired in 2006, as discussed above. The Group reassessed the recoverable amount of the asset and reversed € 5.2 million of the previously recognized impairment loss in the 2008 Financial Statements.

In the fourth quarter of 2008, the Group also recognized an impairment charge of € 0.3 million for the animal housing facility in Bern, Switzerland, that is no longer in use.

Goodwill

Goodwill is reviewed annually or more frequently when changes in circumstances indicate that the carrying amount may be impaired. The discounted net present value calculations are derived from the Group's most recent long range plan, which forecasts the period for the next five years. Beyond this five year window, cash flows are extrapolated based on the estimated terminal growth rate.

Management exercised judgment in determining the segments and the subsequent allocation of the goodwill. In 2008, the Group reorganized its reporting structure in a way that changes the composition of one or more cash-generating units to which goodwill has been allocated, as the Vaccines and Proteins business units were integrated. In the prior year, all goodwill was allocated to the Vaccines Unit. As a result of the change in composition, Management had to reallocate the goodwill and decided to assign all goodwill to the 2006 business acquisitions that led to the recognition of the goodwill. Management decided not to allocate the goodwill to the individual business acquisitions as the operations are integrated and the allocation would be arbitrary.

Valuation of defined benefit plans

Under defined benefit plans, the pension entitlements are calculated using the projected unit credit actuarial method. The pension liability recognized in the balance sheet is the present value of the defined benefit obligation at the balance sheet date, less the fair value of the plan assets after adding or subtracting unrecognized actuarial gains or losses and 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 and any unrecognized past service costs and the fair value of any plan assets are deducted.

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 31 December		
	2008	**2007**	**2006**
Discount rate	3.37%	3.40%	3.32%
Expected return on plan assets	4.53%	4.53%	4.55%
Future salary increase	1.19%	1.22%	1.19%
Future pension increases	0.71%	0.78%	0.66%

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. The following weighted average assumptions were used in determining the fair value of the stock options.

	Year ended 31 December		
	2008	**2007**	**2006**
Risk-free interest rate	4.3%	4.1%	3.6%
Expected dividend yield	–	–	–
Expected volatility	36.7%	33.3%	41.8%
Expected life (years)	4.76	4.25	4.25

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 Dutch 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, as IFRS 2 does not allow updates to the original estimate for market-based conditions during the vesting period. 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 a 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 as of the balance sheet date.

Valuation of inventories

Inventories are stated at the lower of cost and net realizable value. Management exercises judgment in determining the allowance for obsolete inventory. Inventories are usually written down to net realizable value item by item. In some circumstances, however, it may be appropriate to group similar or related items. In these cases, the Group considers numerous items, which include test results by quality control, review by local supply chain, historic scrapping and rejection percentages per product and the current product portfolio. The allowance recognized in 2008 is € 3.2 million (2007: € 6.4 million).

8.13 Corporate income taxes

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 at the balance sheet date. Current income tax relating to items recognized directly

in equity is recognized in equity and not in the income statement. 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 balance sheet date 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 balance sheet date 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 at the balance sheet date.

Income tax relating to items recognized directly in equity is recognized in equity and not in the income statement. Deferred tax assets and deferred tax liabilities are offset if a legally enforceable right exists to offset current tax assets against current tax liabilities and the deferred taxes relate to the same taxable entity and the same taxation authority.

The Group has unrecognised tax carry forward losses of € 172.7 million (2007: € 254.5 million; 2006: € 222.3 million) that are available, with certain restrictions in time, for offset against future taxable profits of the companies in which the losses arise. In the Netherlands, anti-abuse laws may limit our ability to realize our unrecognised tax carry forward losses for an amount up to € 26.2 million.

To avoid the evaporation of unrecognized tax carry forward losses we made an agreement with the Dutch tax authorities about a retroactive change with respect to the valuation of intellectual property for tax purposes. This has reduced our unrecognized tax carry forward losses with an amount of € 72.0 million. Instead we have an unrecognized deferred tax asset in relation to the valuation difference for Intellectual property. The valuation difference will decrease over time and will result in lower taxable amounts in the future.

The unrecognized carry forward losses expire as follows:

Year	Unrecognized carry forward loss in thousands of euro
2011	17,502
2012	21,164
2013	19,153
After 2013	113,966
Unlimited	947
Total	**172,732**

The Company has evaluated evidence impacting the recoverability of its deferred tax assets, which consist principally of tax loss carry forwards. In 2008 we recognized a deferred tax asset for the carry forward losses of Berna Biotech AG. Per the end of the year the deferred tax asset amounted to € 9.0 million.

A summary of our tax charge in thousands of euro

	Year ended 31 December		
	2008	**2007**	**2006**
Current income tax	(3,200)	(811)	(258)
Adjustments current income tax of previous years	7	(5)	(213)
Deferred taxation	11,503	3,024	10,922
Income tax	**8,310**	**2,208**	**10,451**

The reconciliation between the loss for the year multiplied by the applicable tax rate and the actual taxation is as follows:

	Year ended 31 December		
	2008	**2007**	**2006**
Loss for the year before income tax	6,276	(45,118)	(97,649)
At gross weighted average income tax rate	820	12,197	21,337
Adjustments in respect of current income tax of previous years	7	(5)	(213)
Deferred tax assets not recognized	(6,301)	(380)	-
Recognition tax loss carry forwards	9,284	4,072	-
Effect of tax rate changes	3,527	(197)	3,894
Research and development tax credit	2,916	-	-
Other permanent differences	(1,741)	(3,488)	1,271
Effect of current tax losses not recognized as deferred tax assets	(202)	(9,991)	(15,838)
Income tax	8,310	2,208	10,451
Effective income tax rate	(132.4%)	4.9%	10.7%

9 INDUSTRY OVERVIEW

In this Chapter we discuss the development of the biopharmaceutical areas in which we are predominantly active: vaccines and antibodies.

9.1 Vaccines

Vaccines are biological substances that stimulate an immune response which 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.

Scientific progress in vaccines

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. Today, research is underway to develop efficacious and safe vaccines against, among others: viruses, parasites, bacteria and inherited or acquired diseases.

Vaccine formats

A variety of vaccine formats are in use today and others are evolving through ongoing R&D 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.

Vaccine technology development

A large variety of vaccine technologies are under development in an attempt to improve safety and to overall vaccine efficacy. The key objectives of current vaccine technology R&D 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.

9.2 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, which are disease-causing agents such as parasites, viruses and 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 in the areas of genomics and proteomics.

Scientific progress in antibodies

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 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 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.

9.3 Competition in product and technology development

The biotechnology field is one of rapid change and innovation. We expect that this industry will continue to experience significant technological and other changes in the years ahead. We operate in highly competitive markets and we may experience competition from companies that have similar or other technologies and other products or forms of treatment for the diseases we are targeting. We may also experience competition from companies that have acquired or may acquire technology from universities or other research institutions. 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 earlier than we or our licensees do. Other companies are developing products to address the same diseases and conditions that we and our licensees target and may have or develop products that are more effective than those based on our technologies. We also compete with our licensees in developing new products.

Vaccine markets

According to the "Global Vaccine Market Outlook (2007-2010)" published by RNCOS, the growing rate for the global vaccine market will be 16.52% and the global vaccine market is expected to reach $ 21.05 billion by 2010.

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. With a projected compound annual growth of over 16% in the next five years, the industry will emerge as the fastest growing therapy area.

Segment-wise, paediatric vaccines presently dominate the global vaccine market but adult vaccine segments will define the future direction of growth. The cancer vaccine market is presently one of the most lucrative areas for vaccine manufacturers. Overall, cancer vaccines are expected to account for nearly 27% of the total vaccine revenues by 2012. Flu vaccines have huge demand at present and all major vaccine manufacturers are to develop the vaccine.

Owing to lower margins and the mature nature of these markets, the basic and enhanced paediatric markets are expected to show stagnant growth in 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. Analysis of the competitive landscape of the market shows its highly concentrated structure.

The vaccines market is diversified in the type of diseases that are targeted by vaccines. 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 Nobilon.

With respect to vaccines, other companies use alternative non-human expression platform technologies. We are aware of licensed vaccines that are produced in cell substrates such as Madin Darby Canine Kidney cells (**MDCK**) and VERO as well as on production platforms based on embryonated chicken eggs. There are also mouse brain-derived inactivated vaccines that are produced in several Asian countries. We are aware of other human expression technologies for licensed and marketed vaccines, as well as human cell lines supporting products in development.

Antibody markets

Following the success of recombinant proteins, therapeutic monoclonal antibodies (mABs) represent the second wave of innovation created by the biotechnology industry during the past twenty years. According to marketresearcher Datamonitor in 2007 total global mAb sales reached $ 26 billion and are forecast to almost double to $ 49 billion by 2013. Monoclonal antibodies (mAbs) are forecast to act as the key growth segment of the prescription pharmaceutical market.

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

Other biotechnology companies, including UCB Celltech, Genentech and PDL BioPharma, currently generate humanized antibodies, and Cenocor, Biogen IDEC, Medarex, Inc., GenMab, and Regeneron produce human antibodies from transgenic mice. Abbott, MedImmune, MorphoSys AG and Dyax generate fully-human 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.

9.4 Regulations applicable to the biopharmaceutical industry

We operate in a highly regulated industry. Our products require approval by government health authorities before they can be sold, and require significant pre-clinical testing before approval will be granted. Our R&D 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.

Obtaining product approval is a costly and time-consuming process. All of our potential products, and those of our licensees, are either in research or development. Any products we or our licensees develop will require regulatory clearances prior to clinical trials and additional regulatory clearances before being produced and distributed commercially. These regulatory processes are generally stringent and time consuming. We expect the EMEA in the European Union, the FDA in the US, the College ter Beoordeling van Geneesmiddelen 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) 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.

Before marketing a (bio) pharmaceutical product, companies require regulatory approval from the relevant authorities. To obtain this approval, 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. On successful completion of the clinical trials and demonstration that the product can be manufactured in a safe and consistent manner, approval to market the biopharmaceutical may be requested from the EMEA in Europe, the FDA in the US or their counterparts in other countries.

Clinical trials are normally done in three 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.

Our R&D and production activities are undertaken in a number of countries around the world. These activities are subject to strict regulatory requirements of the national and supranational authorities in the countries in which they are undertaken such as those governing the testing, manufacturing and marketing of pharmaceutical products. In most countries, it is necessary to obtain approval to market a pharmaceutical or medical product, the granting of which is subject to a detailed evaluation of data submitted by the applicant relating to the quality, safety and efficacy of the product. Many countries, including member states of the EU and the US, impose extensive testing and data submission requirements and conduct rigorous technical appraisals of product candidates. In addition, different regulatory authorities may impose different conditions upon the marketing of a given product or may refuse to grant approval or require additional data before granting approval to market a product even though the product may have been approved by another regulatory authority. Pre-clinical testing, clinical research and regulatory approval of a pharmaceutical or medical product is a lengthy and costly process.

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 relating to the manufacturing, safety, quality, efficacy or stability, as well as changes in the characteristics, of a product inherent to its biological origin may result in the imposition of restrictions upon the manufacturing and sale of it, including at worst withdrawal of the product from the market and/or the revocation of the relevant regulatory approvals.

9.5 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 or approval.

The WHO Pre-qualification project 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 project does not intend to replace national regulatory authorities or national authorization systems for the importation of medicines.

10 BUSINESS OVERVIEW

10.1 Our history and development

We were incorporated on 9 October 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.

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 turn-key solutions for the production of monoclonal antibodies and recombinant proteins.

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

10.2 Business drivers

Our business strategy is based on the following business drivers:

- Products
- Leveraging presence of our marketed vaccines in public and private markets.

We produce and sell established paediatric, respiratory and travel vaccines. We intend to enhance our position in these markets by highlighting the unique features of these products and by providing outstanding customer service in terms of delivery, reliability and quality and by leveraging our worldwide presence in both public and private markets.

Our core portfolio consists of the following products:

- Quinvaxem, a fully liquid vaccine for protection against five important childhood diseases;
- Hepavax-Gene, a recombinant vaccine against hepatitis B;
- MoRu-Viraten, a vaccine against measles and rubella (all age groups);
- Epaxal and Epaxal Junior, the only aluminium-free and biodegradable vaccine against hepatitis A;
- Vivotif, the only oral vaccine again typhoid fever; □

- Dukoral, the only oral vaccine against diarrhoea caused by cholera and Enterotoxigenic Escherichia Coli (**ETEC**); and

- Inflexal V, the only virosomal adjuvanted influenza vaccine for all age groups.

R&D product pipeline with competitive advantage

We believe that each of our selected products targets unmet medical needs, improves current medications or is otherwise believed to be marketable due to predictive study models and/or perceived favourable regulatory conditions. These products are predominantly based on our PER.C6 technology. In addition, we have various discovery programs to find new vaccine and antibody products.

Besides our portfolio of well known vaccines, we have a pipeline of new potential vaccines and antibodies. Product pipeline programs include vaccines against yellow fever, influenza, tuberculosis, Ebola and Marburg, malaria, HIV, rabies and H5N1 antibodies. Our R&D activities are concentrated in our headquarters in the Netherlands, but we also have R&D facilities in Switzerland and South Korea. Product development is concentrated at our Swiss operations in Bern.

Technologies – ongoing technology licensing programme

We have a broad base of excellent technologies with applicability to vaccines, antibodies, other recombinant proteins and gene therapy. Our licensing programme provides a source of revenue as well as the potential for future, additional revenue in the form of royalties from products developed by our licensees. In areas where we are not developing our own products, we offer our technologies to the biopharmaceutical industry for the development and production of diverse biopharmaceutical products.

We have developed various proprietary technologies such as PER.C6, AdVac, MAbstract, STAR, our virosomal technology and rCTB, as well as our Hansenula polymorpha expression system. We believe our proprietary PER.C6 technology is well suited for the development and large-scale manufacturing of a wide range of biopharmaceuticals including vaccines, monoclonal antibodies, therapeutic proteins and gene therapy products. AdVac is used to develop novel adenoviral-based products. MAbstract can be used to develop human antibodies. Our STAR technology is useful for increasing production output of recombinant antibodies and therapeutic proteins on mammalian cell lines and there are indications that the technology is complementary to our PER.C6 technology.

10.3 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 with the majority of our sales coming in the second half of the financial year. 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 (see Chapter 10.6 “Business Overview - Partners, agreements, investments and other collaborations – Marketing and sales partners” for more details on our partners.)

Vaccine markets

Our core product portfolio currently consists of seven 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, Hepavax-Gene and MoRu-Viraten.

Quinvaxem

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 is 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 South Korea. In October 2008, we announced that we will relocate the South Korean production facility from Yongin City to the Incheon Free Economic Zone. The new facility will enable the further growth and more efficient production of Quinvaxem and Hepavax-Gene.

As Quinvaxem has been pre-qualified by the WHO, it 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 September 2008, we were awarded with new contracts totalling over $ 140 million for our Quinvaxem and Hepavax-Gene paediatric vaccines by supranational organizations. The contracts provide for the supply of these vaccines for the period 2008 - 2009, bringing the total value of the contracts for the period 2007 - 2009 to $ 500 million.

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.

In 2008, the Chinese authorities released Hepavax-Gene for registration and quality control in China. Market researcher Decision Resources estimates that the Chinese HBV drug market will more than double between 2007 and 2012 (from $ 340 million in 2007 to $ 800 million in 2012).

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.

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.

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 million to 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

Our core travel vaccines are Epaxal, Vivotif and Dukoral.

Travel vaccines include all vaccine products that protect against diseases that are not native to the region travellers are from, but are present in the regions to which they travel. Generally, the target population groups for these vaccine products are individuals travelling 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 it can be targeted at multiple markets.

Epaxal

Epaxal is the only aluminium-free and biodegradable HAV vaccine on the market, offering significant advantages in terms of tolerability. It was the first product to be based on the virosome technology developed and patented by the Crucell company, Berna Biotech AG. It induces protective antibody levels within ten 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 year. It is currently licensed in more than 40 countries under the brands Epaxal, HAVpur and VIROHEP-A.

About HAV

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-limiting 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.

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 years 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. It 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, stomach pain, weight loss, loss of appetite, delirium, severe diarrhoea (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 five million people are believed to develop paratyphoid fever annually.

Dukoral

Dukoral is an oral vaccine that protects against cholera and ETEC 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 travellers and is indicated for use in adults and children over two years of age. Pregnant and lactating women may use it. Other than Dukoral there is no cholera and ETEC combination vaccine available in the world.

About Cholera

Cholera is an acute, diarrhoeal 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 traveller's diarrhoea. Approximately 10% of infected persons have a severe case, characterized by profuse watery diarrhoea, 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 parts of Asia, Africa and South America. It spreads via contaminated food and water.

Respiratory vaccines

Our core respiratory vaccine is Inflexal V.

Inflexal V

Inflexal V is a virosomal adjuvanted Influenza vaccine (subunit), based upon the virosome technology developed and patented by the Crucell company, Berna Biotech AG. It is the only adjuvanted flu vaccine licensed for all age groups (from six 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.

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 human beings 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.

Each year approximately 5% to 15% of the world's population contracts influenza and an estimated 250,000 to 500,000 people die annually from influenza-associated complications, according to the WHO. As well as these annual epidemics, a major genetic shift in the influenza virus can occasionally lead to a deadly new virus strain to which the human population does not have immunity, resulting in a global pandemic. Concerns currently exist that a new avian influenza strain (H5N1) endemic among birds in Asia, and showing high pathogenicity for humans, could present a genuine pandemic threat.

Several factors contribute to the rapid growth of the influenza vaccine market. We expect that the threat of a pandemic of avian flu, the ageing of the population in numerous developed countries, national government-sponsored vaccination programs in many countries, higher awareness of the value of a flu vaccination among the public at large, as well as specific production contracts for vaccines that combat strains of pandemic flu and ongoing activities to increase the preparedness for a flu pandemic, will lead to further growth in the seasonal flu markets.

10.4 Research and Development pipeline

Overview

Our product development programs comprise vaccines against yellow fever, influenza, tuberculosis, Ebola and Marburg, malaria and HIV, human monoclonal antibodies against rabies and human monoclonal antibodies against a broad range of influenza.

Overview of our pipeline based on proprietary technologies

Our PER.C6 technology, complemented by our AdVac and MAbstract technologies, drives the development of our product pipeline. 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 core potential products we are developing using our core technologies:

An influenza vaccine, in collaboration with Sanofi Pasteur is being developed using our PER.C6 technology;

Our Ebola and Marburg, malaria and TB vaccine candidates are recombinant vaccines based on PER.C6 technology that also employ AdVac technologies; and

Our candidate rabies and influenza antibodies are generated and produced using our PER.C6 and MAbstract technologies.

Of the potential products we have under development, only our yellow fever vaccine does not use our core technologies.

Overview of our late-stage pipeline

- Yellow fever vaccine

Crucell has developed the yellow fever vaccine, Flavimun, based on a well-established vaccine formerly produced by the Robert Koch institute in Germany. We acquired the rights and know-how for this vaccine against yellow fever from the Robert Koch Institute, which has produced the vaccine since 1963. Over 2.5 million doses of the vaccine have been distributed. The vaccine is safe, highly immunogenic and well tolerated. Protection starts ten days after a single dose and persists for ten years. The product was submitted for registration with the Swiss authorities in the first quarter of 2009. Registration submission in Germany is expected in 2009.

Overview of our early-stage pipeline

The following is a short description of our main potential products in the early-stage pipeline as well as the diseases those products target.

- Influenza

Influenza vaccines were classically produced on embryonated chicken eggs. Currently, cell culture systems are being developed for more efficient influenza vaccine production based on 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 avian strains of influenza that may present a pandemic threat.

- Sanofi Pasteur

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. Since the inception of the collaboration, production processes have been under development, with the production of a GMP master cell bank already completed. Currently, we are working to develop a pandemic flu vaccine as well as an interpandemic, or seasonal, flu vaccine under this contract. A phase II testing 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.

- 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 (the **AERAS**). The Crucell-Aeras TB vaccine programme is focusing on an AdVac based vaccine that can boost the immune response against TB, initially induced by Bacille Calmette-Guérin (**BCG**) vaccine, using our PER.C6 and AdVac technologies.

A first phase I clinical trial, launched in October 2006 in Kansas, US, indicated that the vaccine candidate, AERAS-402/Crucell Ad35, is safe in healthy adults in the US. The preliminary results of a second study, 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. A third phase I study in St. Louis, Missouri, US was launched in December 2007 and focuses on the immunogenicity

and safety of two AERAS-402/Crucell Ad35 boost doses administered at three- to six-month intervals after BCG-priming in healthy adults.

An ongoing study in St. Louis, Missouri, US is evaluating a longer prime-boost interval. The study has been fully enrolled and has discovered no safety issues. Immunological data is expected to be available in the first half of 2009.

In October 2008, Crucell and AERAS announced the start of a phase I clinical trial in Kenya. The main parameters of the study will be to test the safety of the vaccine candidate in healthy adults, all of whom have been previously vaccinated with the BCG vaccine and a subset of whom have evidence of having been exposed to TB. This study is fully enrolled and now in its follow-up segment, with no safety issues identified. The companies also started the enrolment of the first phase II study of the vaccine candidate. The study is being conducted in Cape Town, South Africa by the University of Cape Town Lung Institute in conjunction with the South African Tuberculosis Vaccine Institute. No evidence of an unacceptable safety issue has been found in its dose escalation design.

- About tuberculosis

TB is a major cause of illness and death worldwide, especially in Asia and Africa, with over nine million new cases diagnosed in 2006. According to the WHO, an estimated 1.7 million people died from TB in 2006. One-third of the world's population has been infected with the TB bacillus and current treatment takes six to nine 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.

- Ebola and Marburg

Crucell is developing an Ebola vaccine in collaboration with the Vaccine Research Center (the **VRC**) of the National Institute of Allergy and Infectious Diseases (**NIAID**).

In May 2002, we entered into a Collaborative Research and Development Agreement (**CRADA**) with the VRC 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 August 2002, the CRADA was extended to cover vaccines against Marburg and Lassa infections.

In experiments conducted by the VRC together with the US Army Medical Research Institute of Infectious Diseases (the **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 US NIH patents to develop and commercialize recombinant vaccines against Ebola.

In October 2008, we secured a NIAID/ US 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 triggered at the discretion of the

NIAID for an additional $ 40 million. The phase I study of an Ad5-based Ebola vaccine, being developed in partnership with the VRC, 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.

- 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's 'A' list of bioterror agents, together with smallpox and anthrax.

- 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. The study showed that a single administration of a prototype AdVac vaccine, provided protection against the specific parasite. Since March 2004, we have collaborated with the NIAID for the support of the development of our candidate malaria vaccine. In September 2006, we extended our collaboration with the NIAID by signing a clinical trial agreement.

In partnership with the NIAID, the Company'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. The first three groups have been enrolled and ongoing safety monitoring has revealed no significant safety concerns to date, but formal analysis awaits unblinding of the data. Further updates on this programme are expected in the second quarter of 2009.

- 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 in 300 million to 500 million individuals worldwide according to the WHO and causing 1 million to 3 million deaths every year. 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% to 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 travellers.

- 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 US 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 recombinant HIV vaccine that Crucell is jointly developing with the Beth Israel Deaconess Medical Center, using adenovirus serotype 26 (**Ad26**) 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, US and is focused on assessing the safety and immunogenicity of the vaccine. Enrolment is currently ongoing.

- 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 programme on HIV/AIDS and the WHO estimate that AIDS has killed more than 25 million people since it was first recognized on 1 December 1981, making it one of the most destructive pandemics in human history.

There is currently 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 (**ARV**) 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.

Antibodies

- Rabies monoclonal antibody combination

We are developing a human monoclonal antibody combination for the post-exposure treatment of rabies. The use of Crucell's MAbstract technology resulted in a combination of two human anti-rabies antibodies. The monoclonal antibodies are produced on Crucell's PER.C6 technology.

Post-exposure treatment for rabies, when given timely transpose, is 100% effective and involves the use of a vaccine plus antibodies. Neither vaccine nor antibodies are effective independent of one another. Current supply and quality of rabies vaccine is sufficient, but anti-rabies antibodies (Human Rabies Immune Globulin (**HRIG**) and Equine Rabies Immune Globulin (**ERIG**)) are widely recognized as being insufficient in quality and supply, and pose safety concerns because they originate from human or equine serum. Market opportunities for rabies treatments are projected to grow significantly as the customer base grows in affected countries such as India and China.

We have developed the human monoclonal antibody combination in collaboration with the Thomas Jefferson University (**TJU**) based in Pennsylvania, US and the Center for Disease Control (**CDC**) in Georgia, US using MAbstract and PER.C6 technology. Our rabies monoclonal antibody combination demonstrated protection at least equivalent to HRIG in pre-clinical trials.

In December 2007, we signed an exclusive collaboration and commercialization agreement with Sanofi Pasteur for our rabies monoclonal antibody combination to be used in association with rabies vaccine for post-exposure prophylaxis against this disease. We will continue to perform the development activities and will be responsible for the manufacturing of the final product and will retain exclusive distribution rights in Europe, the rights to sell to supranational organizations such as UNICEF and co-exclusive distribution rights in China.

The programme has been granted a Fast Track designation by the FDA.

Phase I clinical trials demonstrated that the antibody product is well tolerated, provides the expected immediate passive neutralizing activity and that it can be safely administered in combination with a rabies vaccine without interfering with the vaccine's ability to induce an active immunity.

Phase II clinical trials began in the US in March 2008. In October 2008, the positive preliminary results of the US study were presented. No serious adverse events were reported and the study confirmed the neutralizing activity of the antibody product against the rabies virus. In May 2008, a second phase II clinical study began in the Philippines and was completed before year-end 2008. Final data from this study are expected to become available in the first half of 2009.

An additional phase II study in healthy adults evaluating the Crucell's monoclonal antibody in combination with a rabies vaccine started in February 2009.

- 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 ten million people a year are treated after exposure to rabies. Some 40,000 to 70,000 people are thought to die of the disease each year, mainly in China and India, according to various medical publications.

- 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 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 the most current anti-influenza drug 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.

10.5 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, from grants and government subsidies obtained to support the development of our technologies and potential products and from service fees earned under development contracts with our partners. We intend to increase our revenues in the future from initial license fees, license maintenance fees and milestone and royalty payments from products that our licensees develop using our technologies.

Our business development strategy historically involved 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. For some of the contracts we provide services, for which we are paid at different rates.

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, their joint venture in Massachusetts, US (**PERCIVIA**) was scaled up to 250 litres by DSM Biologics scientists at their GMP facility in Groningen, the Netherlands. They successfully achieved eight grams per litre for an IgG antibody expressed by PER.C6 cells using chemically defined cell culture medium in a single-use bioreactor. In June 2008, the Company reported record-breaking protein yields of 27 grams per litre using DSM's innovative XD™ technology.

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 a high virus titre, 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 0inserted 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-scale 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 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 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 as per year end 2008 please see the Appendix "Overview Licensees and Partners" to the annual report including the 2008 Audited Financial Statements.

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.

AdVac technology

Overview

Crucell has been a key player in the development of adenoviral-based vaccines for more than five years, resulting in the availability of proprietary AdVac vectors. Crucell has 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 adenoviruses 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 hemorrhagic fevers (Ebola, Lassa, Marburg), malaria, TB, HIV/AIDS and hepatitis C (**HCV**). 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

Overview

Our MAbstract technology can be applied to the discovery of novel drug targets and the identification of human 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

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.

Multiple companies and licensees are investigating whether the STAR technology can increase production yields of biological substances. 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.

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 the antibody or other therapeutic proteins of those generated without STAR.

Virosomal technology

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 aluminium salt derivatives, which are known to cause adverse reactions such as irritation and inflammation at the injection site. 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.

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;
- Virosomes stimulate both arms of the immune system, eliciting both antibody and cellular immune responses, against inserted immune stimulatory proteins derived from human pathogens;
- Virosomes are completely biodegradable and can exert an immune response via different routes of administration; and
- Virosome technology is used in the manufacture of several of Crucell's registered products where it has an excellent safety record.

Other proprietary technologies

In addition to our core proprietary technology platforms we employ 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 (CTB) sub-unit technology

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 state-of-the-art GMP manufacturing facility for recombinant CTB. The production system is designed so that CTB is produced completely devoid of the toxins.

10.6 Partners, agreements, investments and other collaborations

Strategic partners

In addition to our own R&D 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.

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 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 had 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 in South 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.

MedImmune

In October 2007, we entered into an exclusive license and research collaboration with MedImmune to further develop and commercialize bacterial antibodies primarily for the treatment and prevention of hospital-acquired bacterial infection. Crucell discovered these antibodies with use of the MAbstract-technology.

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. The development activities will take place in our facilities in Bern, Switzerland. Wyeth will be responsible for the overall clinical development of the vaccine.

Ortho-McNeil-Janssen Pharmaceuticals (an affiliate of Investor)

On 28 September 2009, we have entered into the Collaboration Agreements with Ortho-McNeil-Janssen Pharmaceuticals (an affiliate of Investor) concurrently and in relation with the Issuance as described on the cover page of this Prospectus and in Chapter 1.4 "Summary – Summary of the terms of the Issuance". These Collaboration Agreements consist of (i) a flu-mAb collaboration agreement with regard to the discovery, development and commercialization of antibodies against influenza A virus and (ii) an agreement on the innovation, development and commercialization of novel antibodies, vaccines and/or small molecules having pharmaceutical properties useful in preventing, treating and diagnosing various disease indications, limited to a number of targets.

Under the flu-mAb collaboration, Crucell and Ortho-McNeil-Janssen Pharmaceuticals or its Affiliates will share responsibilities to develop a universal flu-mAb product targeting all influenza A strains, including H1N1 strains (which cause seasonal flu and the current pandemic) and the H5N1 or 'bird flu' avian strain. Crucell will be responsible for research and development through Phase IIa of the influenza antibodies it has already discovered, as well as newly discovered influenza antibodies that emerge from the collaboration. Ortho-McNeil-Janssen Pharmaceuticals or its Affiliates will be responsible for late-stage development of the flu-mAb product from Phase IIb onward.

Under the long-term innovation collaboration, Ortho-McNeil-Janssen Pharmaceuticals or its Affiliates and Crucell will jointly work to discover and develop a universal flu vaccine for the prevention of

influenza, as well as antibody and/or vaccine products against up to three additional infectious or non-infectious disease targets to be selected after exploratory research.

Other collaborations and agreements

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 that 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 as per year end 2008 please see the Appendix "Overview Licensees and Partners" to the annual report including the 2008 Audited Financial Statements.

10.7 Our equity investments

Subsidiaries

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 Chapter 10.10 "Business Overview - Group structure".

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

On 3 July 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 of € 1.6 million on the sale in 2008.

For a complete overview of our associates and joint ventures please see "5.9 Investments in associates and joint ventures" in the 2008 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. Galapagos is listed on the Euronext Brussels and 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 5.8% of Galapagos as of 31 December 2008 (2007: 5.8%).

10.8 Marketing and sales partners

We have our own sales and marketing infrastructure in our markets in the Benelux, Switzerland, Italy, Spain, Scandinavia, US and Canada, Argentina, China, South Korea, Indonesia and Vietnam. On September 30, 2009 the Company announced the launch of its own dedicated marketing and sales organization in the United Kingdom by acquiring an experienced team, to further strengthen its vaccine sales position in one of the largest vaccine markets in Europe. Crucell UK Limited will market and sell Crucell's travel vaccines Epaxal®, Vivotif® and Dukoral® as well as its registered virosomal adjuvanted influenza vaccine Inflexal® V. Distribution of the travel vaccines will start immediately and 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 in terms of current sales value 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**)	a number of SSI products in Spain and Sweden
Green Cross Corporation Korea	Green Cross Corporation's Japanese encephalitis vaccine in Europe
Netherlands Vaccine Institute (**NVI**)	NVI (Belgium, Netherlands, Luxembourg)
Talecris Biotherapeutics	partner of Talecris's product Prolastin in nine Western European countries

In addition we have developed a network of companies that market and sell our products. The most significant collaborations in terms of current sales value are:

Our Partners:	*Marketing, sales and distribution partner for:*
Zuellig	partner for our flu vaccine in China

Baxter International Inc.	partner for certain vaccines in Austria, Germany, Greece and Russia
Infectopharm Germany	partner for our flu vaccine in Germany
Novartis–Behring	partner for our travel vaccines in Germany
Sanofi Pasteur	partner for Dukoral in Canada, Australia and a number of other countries outside Europe and the US
Sanofi Pasteur MSD	partner for our flu vaccine in the UK
Kedrion	partner for our flu vaccine in Italy

10.9 Intellectual property

Overview

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 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 who file, prosecute, defend and enforce patent rights and manage our patent portfolio. Our patent portfolio comprised 1677 active cases (i.e. granted patents in force or pending patent applications) as of 31 December 2008. 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 31 December 2008, 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.

2008 Patent filings	**Pending**	**Granted**	**Active**
Vaccines	259	367	626
Antibodies	141	77	218
Technology	268	344	612
Gene Therapy	50	171	221
Total	**718**	**959**	**1,677**

Patent filings

In 2008, we filed patent applications for four new inventions, in the fields of vaccines and technology. Our new filings in the vaccine field in 2008 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 R&D, no new filings were made in that area during 2008.

We maintain a geographically diversified filing strategy, depending on our technological and business needs, as well as our view of long-term economic trends and developments in legal systems in various parts of the world. As of 31 December 2008, we had 64 pending applications in the EU, 110 pending applications in the US, 21 international patent applications (so-called Patent Cooperation Treaty (**PCT**) applications) and 523 applications in the rest of the world.

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 applications 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 31 December 2008, we owned or co-owned 601 granted patents in the EU territory, 83 patents in the US and 275 patents in the rest of the world.

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

Epaxal and Inflexal V

Epaxal and Inflexal V are the two virosomal 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 South Korea, we have several platform technologies and consequently our intellectual property 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 South 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 from the Group

In 2005, each of Probiogen, CEVEC Pharmaceuticals and Serono filed oppositions with the European Patent Office against one or more of our PER.C6 patents. All PER.C6 technology patents were upheld after first instance opposition proceedings. The PER.C6 patents pertaining to protein and virus production are no longer subject to opposition proceedings. The basic PER.C6 patent is currently under appeal, with Crucell as the only appellant and CEVEC Pharmaceuticals as party as of right. The outcome of appeal proceedings can only improve Crucell's position.

Cell Genesys has filed an opposition against our European patent related to our AdVac technology. Following the withdrawal of Cell Genesys from the opposition a swift resolution of the maintain opposition in Crucell's favour is now underway.

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 advisers, 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 from competitors

Our subsidiary Berna Biotech Korea Corp. (formerly Green Cross Vaccine Corporation) and our partner Novartis (formerly Chiron) lodged opposition against a patent of GSK in South Korea. The patent relates to multivalent vaccine formulations, such as our pentavalent vaccine Quinvaxem. In response to the opposition, the patent was revoked by the South Korean Intellectual Property Office in December 2004 on the grounds that the subject-matter claimed in the patent lacks novelty. GSK appealed that decision to the South Korean Patent Court. After a hearing which took place in April 2006, the South Korean Patent Court dismissed the appeal in June 2006. GSK appealed this decision before the South Korean Supreme Court. In 2008, the South Korean Supreme Court confirmed the decision by the South Korean Patent Court and declared the patent to be invalid. This decision is final.

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.

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, is currently under opposition before the patent office and a definitive outcome on the validity of the patent is expected to take a number of years. A negative outcome of this opposition proceeding 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 if GSK were to prevail in infringement proceedings against us, this would adversely affect our business.

Technology licenses from third parties

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.

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.

Technology licenses to third parties

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.

10.10 Group structure

The Company is the holding company of a number of directly held operating companies. Our most significant subsidiaries, joint ventures and associates are:

Name	Legal seat ownership	Country	Ownership
Subsidiaries (consolidated)			
Crucell Holland B.V.	Leiden	the Netherlands	100%
U-BiSys B.V	Utrecht	the Netherlands	100%
ChromaGenics B.V	Amsterdam	the Netherlands	100%
Berna Biotech AG	Bern	Switzerland	100%
Berna Biotech España SA	Madrid	Spain	100%
Berna Biotech Italia Srl	Milan	Italy	100%
Berna Rhein B.V.	Leiden	the Netherlands	100%
Berna Biotech Korea corp.	Seoul	South Korea	100%
Crucell Holding Inc.	Wilmington, DE	United States	100%
Crucell Vaccines Inc.	Wilmington, DE	United States	100%
Crucell Biologics Inc.	Wilmington, DE	United States	100%
SBL Vaccin AB	Stockholm	Sweden	100%
Crucell UK Limited	London	United Kingdom	100%
Joint Venture (not consolidated)			
Percivia LLC	Cambridge, MA	United States	50%
Associated company (not consolidated)			
ADImunne corp.	Taipei	People's Republic of China	11.8%

10.11 Property, plant and equipment

Our corporate offices and research activities are located in facilities of approximately 8,700m² in Leiden, the Netherlands. The section of this building that we use in Leiden includes 3,500m² of laboratories, with BSL 1, BSL 2 and BSL 3 labs. The remainder of the main building is divided into 2,800m² of office space and 2,400m² for storage, technical areas, washrooms, waste destruction and sterilization. In addition, we lease 1,200m² of space adjacent to the corporate main building.

In 2008, the construction of the Valerio building, which was named after our co-founder Dinko Valerio, was completed. The Valerio building is a GMP process technology center of 5,400m² in Leiden. 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 laboratory activities to be conducted there. The facility has received approval from the Dutch government to produce material for use in humans. Extensive precautions will be taken to ensure safety and continuity of operations. Product quality will be strictly monitored, maintained and administered in-house.

Since our 2006 acquisitions, we also have office space, laboratories, production facilities, pre-clinical facilities and storage space in Switzerland, Spain, Sweden, South Korea and Italy.

The following sets out information regarding our main facilities outside the Netherlands.

Bern, Switzerland (owned)

We have two facilities located in the canton of Bern. These facilities are FDA/WHO/EMEA approved and are the primary sites for the manufacturing of Inflexal V, Vivotif, MoRu-Viraten and Epaxal. The combined facilities have a floor space of 45,000m², 33,000m² 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.

In addition to the manufacturing, the facilities also have all the necessary support capabilities including clinical affairs, regulatory affairs, quality control, quality assurance, operations, finance and process development.

The process development group has a pilot plant of approximately 2,500m². 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 as well as conducting CMO activity for one of our partners.

Seoul, South Korea (leased)

Our manufacturing facilities in South Korea are Korea Food and Drug Administration/WHO approved and are used primarily for the production of Quinvaxem and Hepavax-Gene and for formulating and filling vials. The facilities include 3,201m² of production and development space, 1,305m² of storage space and 1,818m² of office space.

In October 2008, we announced that we will relocate the South Korean production facility from Yongin City to the Incheon Free Economic Zone. The investments in the new facility are expected to total approximately € 50 million, with the majority of spending in 2009. We entered into a mortgage loan facility in South Korea for an amount of KRW 50 billion to partly finance the investments in the new South Korean facility in 2009.

Madrid, Spain (owned)

We have our main centre for filling and packaging operations in Madrid as well as local distribution. The facility is EMEA-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 2,130m² of manufacturing space, 1,000m² of office/laboratory space and 2,610m² of warehousing.

Stockholm, Sweden (leased)

In Sweden, our manufacturing facilities are EMEA/WHO-approved and are used for the production of Dukoral and the recombinant protein rCTB. The manufacturing capabilities consist of large-scale GMP manufacturing of bulk, comprising both bacterial and mammalian systems, formulation and filling, visual inspection and packaging in vials. The site has a total of 4,866m² of GMP development and production space, 5,990m² storage space and 2,662m² 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 our organization. The Group is now going through a feasibility study to determine the scope and timing of the move.

In 2008, € 15.8 million was invested in property, plant and equipment compared with € 27.2 million in 2007. The investments in 2008 mainly related to our new South 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.

In 2007, € 27.2 million was invested in property, plant and equipment compared with € 20.3 million in 2006. The investments in 2006 and 2007 mainly related to our new GMP production facility in Leiden, the Netherlands and investments in our facilities in Bern, Switzerland.

11 MANAGEMENT BOARD, SUPERVISORY BOARD AND EMPLOYEES

This Chapter contains a summary of the relevant information concerning the Management Board, the Supervisory Board as well as a highlight of certain relevant provisions of Dutch corporate law and the Articles of Association. This Chapter further includes a brief summary of information concerning employees, incentives, co-determination and pension plans.

11.1 General

We have a two-tier board structure consisting of a management board and a supervisory board. The Management Board is the Company's executive body and is responsible for our day-to-day management and our strategy, policy and operations. The Supervisory Board supervises the Management Board's management and the general course of affairs in the Company and the business connected with it, and advises the Management Board. The Supervisory Board's approval is required for certain important decisions of the Management Board.

11.2 Management board

Management board practices

Our Management Board manages our general affairs and business and is responsible for our strategy under the supervision of our Supervisory Board. The Management Board may perform all acts necessary or useful for achieving the Company's corporate purposes, except for those expressly attributed to the General Meeting or the Supervisory Board as a matter of Dutch law or pursuant to the Articles of Association.

The Management Board as a whole is entitled to represent the Company. Additionally, each member of the Management Board is solely authorised to represent the Company.

Our Supervisory Board determines the size of the Management Board after consultation with our CEO.

The General Meeting appoints the members of our Management Board from a list of candidates nominated by our Supervisory Board. If the list contains the names of at least two persons, it forms a binding nomination. However, the General Meeting 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 position within three months after a vacancy occurs, our General Meeting 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 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.

Each member of the Management Board may be suspended or removed by the General Meeting 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 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, which suspension may be terminated at any time by the General Meeting.

A suspension may be extended but may not last more than three months. If no decision has been taken in respect of the termination of the suspension or dismissed, the suspension will terminate.

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.

Our Management Board has to adopt 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.

Under our Articles of Association, the Management Board requires prior approval of the Supervisory Board for:

- all transactions between the Company and persons who hold at least 10% of the Shares that are of material significance to the Company and/or such persons;
- a resolution on the operational and financial aims of the Company, the strategy designed to achieve the aims, and the parameters to be applied in relation to the strategy;
- all transactions in which there are conflicts of interest with members of the Management Board that are of material significance to the Company and/or the relevant members of the Management Board;
- all transactions in which there are conflicts of interest with Supervisory Board members that are of material significance to the Company and/or the relevant Supervisory Board members;
- expanding the affairs of the Company with a new line of business and closing down the business of the Company or any part thereof, including a transfer of ownership or a transfer of the beneficiary use thereof;
- participating, or otherwise taking an interest in or acceptation or disposal of the management of other business enterprises and terminating or modifying such participation or interest;
- entering into, terminating and amending joint venture and pooling agreements;
- acquiring fixed business assets for an amount as determined by the Supervisory Board and notified to the Management Board, each acquisition to be considered separately; and
- performing any legal acts other than referred to in this paragraph, if the interest or value of such acts to the Company exceeds an amount as determined by the Supervisory Board and notified to the Board of Management or by which the Company shall be bound for a period exceeding one year.

The Supervisory Board is entitled to require further resolutions of the Board of Management to be subject to its approval and to amend the amounts involved in resolutions for which the approval of the Supervisory Board is required.

Under Dutch law, resolutions of the Management Board relating to an important amendment of the identity or the character of the Company, require prior approval of the General Meeting which includes: (i) the transfer of (nearly) the entire business of the Company to a third party; (ii) the entering into or

breaking off of long-term co operation of the Company or a subsidiary with another legal entity or company or from being a fully liable partner in a limited partnership (*commanditaire vennootschap*) or general partnership (*vennootschap onder firma*), if this co-operation or termination is of major significance for the Company; and (iii) the acquisition or disposal of a participation in the capital of a company of at least one-third of the sum of the assets of the Company as shown on its balance sheet.

Management Committee

The Company has a Management Committee. The Management Board determines the number of members of the Management Committee, provided that the company secretary will be one of them.

The Management Committee advises the Management Board in strategic, general managerial and executive matters and assists the Board of Management in implementing these matters under the final responsibility of the Board of Management.

Members of the Management Committee must be appointed and dismissed by the Board of Management. The appointment and removal of members of the Management Committee shall require the approval of the Supervisory Board.

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 us and a notice period of three months upon termination by the individual. Nominations for a seat on the Management Board members are for periods 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.

Management board members and functions

Pursuant to the Corporate Governance Code, members of the Management Board are allowed to hold a maximum of two Supervisory Board positions in other listed companies. The members of the Management Board did not hold any such positions in 2008.

The name, date of appointment and position of the members of our Management Board are

Name	Position	Member since	Date of re-appointment	End of current term
Ronald Brus	Chairman of the Management Board, President and Chief Executive Officer	2004 (1997) (1)	Reappointed on 30 May 2008	2012
Leonard Kruimer	Chief Financial Officer	2005 (1998) (1)	Reappointed on 30 May 2008	2012
Cees de Jong	Chief Operating Officer	2008 (2007) (1)	Reappointed on 30 May 2008	2012
Jaap Goudsmit	Chief Scientific Officer	2004 (2001) (1)	Reappointed on 30 May 2008	2012

(1) Dates in brackets indicate start of employment with the Company.

Mr. Ronald Brus has been 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 with us. 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 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 Master's degree in Business Administration from 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 with responsibility 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 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 has been a member of the Management Board since January 2004. He was Senior Vice President Vaccine Research from September 2001 until July 2002 and has been 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 Centre 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 and the founding co-chairman of the European Vaccine Effort against HIV/AIDS. Since 1989, he has been a professor at the University of Amsterdam and the Academic Medical Centre. He holds an MD and a PhD from the University of Amsterdam. Mr. Goudsmit is a Dutch citizen.

The business address of the members of our Management Board and the Management Committee is the same as the address of our principal executive office in Leiden, the Netherlands.

The Management Committee consists of the members of the Management Board and Mr. René Beukema and Mr. Arthur Lahr.

Mr. René Beukema is 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. Mr. Beukema has not held an executive, managerial or supervisory position in any other company or limited partnership in the last five years.

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 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. Mr. Lahr has not held an executive, managerial or supervisory position in any other company or limited partnership in the last five years.

Potential conflicts of interests

Other than the loans as described in Chapter 13.3 "Related Party Transactions – Transactions with members of the Management Board, Supervisory Board and employees", the Company is not aware of any potential conflicts between any duties of the members of the Management Board and the Management Committee and their private interests and/or other duties.

11.3 Supervisory board

Supervisory board practices

The Supervisory Board, which consists solely of independent directors, supervises the management of the Management Board and the general course of affairs of the Company and the business connected with it. In the execution of their duties, the members of the Supervisory Board must be guided by the best interests of the Company and its stakeholders.

Our Articles of Association provide that the Supervisory Board must consist of at least three members. Our Supervisory Board determines the exact number of members of the Supervisory Board after consultation with our CEO.

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 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. 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 can override these binding nominations by a vote of an absolute majority of the votes cast. This vote must be cast in a General Meeting representing 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 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 taken by an absolute majority of the votes cast in a General Meeting 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 passed by an absolute majority of the votes cast. This vote must be cast in a General Meeting representing 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.

A suspension may be extended but may not last more than three (3) months. If no decision has been taken in respect of the termination of the suspension and the member is not dismissed, the suspension will terminate.

The General Meeting determines the Supervisory Board members' compensation. In contrast to the provisions of the Code, until the end of our 2004 fiscal year we paid our Supervisory Board members in options on our ordinary shares as well as in cash. Starting in 2005, we began paying them 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.

Our Supervisory Board appoints its own chairman and 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. The company secretary assists the Supervisory Board.

Passing Supervisory Board decisions requires an absolute 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 Supervisory Board reports to the General Meeting with regard to our corporate governance, its structure and 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 the daily business of the Company 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 resolutions of our Management Board which are described in Chapter 11.2 "Management Board, Supervisory Board and employees – Management Board" above. In addition, our Supervisory Board may give our Management Board written notice of other corporate actions that it wishes to approve.

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.

Supervisory board members and functions

Name	Age	Position	Member since	End of current term
Jan Oosterveld	65	Chairman	2004	2010
Phillip Satow	67	Member	2000	2013
Claes Wilhelmsson	70	Member	2003	2011
Seán Lance	62	Vice-Chairman	2004	2011
Arnold Hoevenaars	60	Member	2005	2013
Steve Davis	52	Member	2008	2012
Floris Waller	50	Member	2009	2013

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 on 3 June 2004. He retired from Royal Philips Electronics N.V. on 1 April 2004, after an international career of 32 years. At his retirement he was responsible for Corporate Strategy, Corporate Alliances and the joint ventures with LGE, South Korea, relating to Cathode Ray Tubes and Liquid Crystal Displays. In the latter responsibility, he was Chairman of the board of LG Philips Ltd, which went public in April 2004, and Vice-chairman of the board of LG Philips Displays B.V. He was also the CEO of Philips Asia Pacific. He graduated with a

degree in mechanical engineering from the Technical University Eindhoven and holds an MBA from the Instituto de Estudios Superiores de la Empresa (**IESE**) in Barcelona. He was appointed Professor at IESE in 2003. He is also a member of the board of Barco, Kortrijk, Belgium, Cookson Group, London, U.K., Candover, London, U.K. and Continental, Hanover, Germany. Mr. Oosterveld is a Dutch citizen.

Mr. Phillip Satow has served as a member of our Supervisory Board since our incorporation. He worked for 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 from 1999 to 2005, Mr. Satow is a former board member of Eyetech Pharmaceuticals Inc. Mr. Satow 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 currently a member of the board of directors of Noven Inc. 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 Gothenburg 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 CEO 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. 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 lecturer in Intellectual Property at the University of Washington Law School. He recently served as the Interim CEO of the Infectious Disease Research Institute and is now chairman of its board of directors. Previously, Mr. Davis was CEO of Corbis Corporation and he presently acts as a senior adviser to the 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 centres. He also holds board positions with Intrepid Learning Solutions, The Seattle Foundation and Global Partnerships. Mr. Davis holds a Bachelor of Arts degree from Princeton University, a Master of Arts degree 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 the Supervisory Board in June 2009. Floris Waller was born on 21 December 1958 in Leiden, the Netherlands. Mr. Waller is a chartered accountant in the Netherlands, and his previous positions include, among others, various senior finance and operations positions from 1984 through 1999 at Unilever N.V./Plc. From 1999 through 2008 he was a member of the management board and Chief Financial Officer of Corporate Express N.V. (previously named

Buhrmann). Mr. Waller was a member of the supervisory board of Univar N.V. and served on its audit committee from 2005 through 2007. Mr. Waller is currently member of the management board and Chief Financial Officer of Pon Holdings B.V., and he holds a doctoral and post doctoral degree in accountancy from the Erasmus Universiteit Rotterdam in the Netherlands. In order to familiarise himself with the Company he has been attending our Supervisory Board meetings as an observer since September 2008. Mr. Waller is a Dutch citizen.

The business address of the members of our Supervisory Board is the same as the address of our principal executive office in Leiden, the Netherlands.

Potential conflicts of interests

The Company is not aware of any potential conflicts between any duties of the members of the Supervisory Board and their private interests and/or other duties.

Supervisory Board committees

The Supervisory Board appoints from among 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.

(a) Audit Committee

Arnold Hoevenaars (chairman), Seán Lance and Floris Waller

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 and for securing and monitoring our external auditors' involvement in that process. 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.

(b) Remuneration committee

Phillip Satow (chairman), Claes Wilhelmsson, Jan Oosterveld and Steve Davis

The Remuneration Committee advises on policies and reviews and determines objectives relevant to the remuneration of the members of the Management Board and members of the Management Committee. The Remuneration Committee evaluates the performance of members of the Management Board and Management Committee in view of these objectives and advises on the remuneration of the members. In advising on short and long-term incentive remuneration, 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 remuneration 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 set the remuneration packages for members of the Management Board and Management Committee at competitive levels. Bonuses are paid to members of the Management Board linked to the 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 remuneration and benefit policies for all of our employees.

(c) Nomination committee

The Nomination Committee consists of all of the Supervisory Board members. This committee (i) draws up selection criteria and appointment procedures for members of the Supervisory Board and the Management Board, (ii) periodically assesses the size and composition of the Supervisory Board and the Management Board and makes proposals of nominees to the Supervisory Board, (iii) periodically assesses the functioning of individual members of the Supervisory Board and the Management Board, and reports on this to the Supervisory Board and (iv) 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.

(d) Scientific Advisory Committee

Claes Wilhelmsson (chairman) and Steve Davis

The Scientific Advisory Committee consists of one Supervisory Board member who is independent within the meaning of the NASDAQ listing rules. This committee is responsible for, among other things, reviewing progress in our R&D activities. The committee reports to the Supervisory Board on a regular basis.

11.4 Remuneration

Remuneration of the members of the Management Board and other members of the Management Committee

The remuneration of the individual members of our Management Board and other members of the Management Committee during 2008**,** excluding stock options, was as follows:

2008 (in thousands of euro)					
Name	**Salaries**	**Bonuses [1]**	**Pension costs [2]**	**Other costs [3]**	**Total**
R.H.P. Brus	433	373	77	—	883
L. Kruimer	292	168	62	13	535
C. de Jong (as of 31 May 2008) [4]	184	119	27	7	337
J. Goudsmit	350	122	94	19	585
Total Management Board	**1,259**	**782**	**260**	**39**	**2,340**
R. Beukema	257	148	28	0	433
A. Lahr	260	117	28	0	405
Totals Management Committee	**1,776**	**1,047**	**316**	**39**	**3,178**

(1) Bonus expense includes the incentive plans to which the Management Board is entitled as at 31 December 2008. The bonus expense excludes option exercises.

(2) "Pension Costs" include pensions, social security costs and disability insurance.

(3) "Other costs" include company cars.

(4) Cees de Jong's remuneration for the year 2008 is included pro rata as of 31 May 2008.

Remuneration of the Supervisory Board

Due to the fact that we operate on a global scale with many of our supervisory directors used to the international arena, we offer remuneration to our supervisory directors in accordance with customary practice in the biotechnology sector.

From 2008 and onwards, remuneration for all Supervisory Board members consists of a fixed fee in cash and an annual share grant. The fixed fee in cash ranges from € 34,000 to € 44,000 per Supervisory Board member. In addition, the chairman of the Supervisory Board is awarded annually a net allowance of € 5,000 that is grossed up for taxation purposes. The annual share grant awarded to each member of the Supervisory Board shall equal 2,500 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. Instead of the share grant, a Supervisory Board member may also choose to receive a cash amount equalling the value of 2,500 shares at the date of grant minus 25%.

During 2008 the individual members of the Supervisory Board were entitled to receive the following remuneration (excluding share-based payments – see information below on stock options and performance stock):

Name	**Year ended 31 December 2008**
J.P. Oosterveld[(1)]	54.2
A. Hoevenaars	35.0
S.P. Lance	34.0
P.M. Satow	35.0
C.E. Wilhelmsson	35.0
S. Davis	34.0
D.S. Koechlin[(2)]	12.5
F. Waller[(3)]	—
Totals	**239.7**

(1) Mr. J.P. Oosterveld was appointed Chairman on 2 June 2006.

(2) Mr. D.S. Koechlin was appointed member of the Supervisory Board on 2 June 2006, but has attended meetings since January 2006. Mr. D.S. Koechlin resigned from the Supervisory Board on 30 May 2008.

(3) Mr. F. Waller was appointed member of the Supervisory Board on 5 June 2009.

11.5 Equity holdings

Options held by members Management Board and other members of the Management Committee

The Management Board members held the following options for the period ended 30 June 2009:

Name of holder	Options held on 31 December 2008	Year of expiration	Exercise price	Granted 2009	Exercised 2009	Forfeited 2009	Options held on 30 June 2009
R.H.P. Brus	250,000	2009	9.4	—	(250,000)	—	0
	200,000	2011	3.49	—	—	—	200,000
	90,000	2011	2.64	—	—	—	90,000
	125,000	2011	5.94	—	—	—	125,000
	300,000	2013	12.23	—	—	—	300,000
	0	2016	10.82	36,170	—	—	36,170
L. Kruimer	30,000	2011	3.49	—	—	—	30,000
	125,000	2011	5.94	—	—	—	125,000
	150,000	2013	12.23	—	—	—	150,000
	0	2016	10.82	19,490	—	—	19,490
C. de Jong	185,000	2012	14.58	—	—	—	185,000
	200,000	2013	12.23	—	—	—	200,000
	0	2016	10.82	20,655	—	—	20,655
J. Goudsmit	85,000	2009	9.4	—	85,000	—	0
	125,000	2011	5.94	—	—	—	125,000
	150,000	2013	12.23	—	—	—	150,000
	0	2016	10.82	23,388	—	—	23,388
R. Beukema	80.000	2011	3.49	—	—	—	80.000
	75.000	2011	5.94	—	—	—	75.000
	85.000	2009	9.40	—	85.000	—	0
	150.000	2013	12.23	—	—	—	150.000
	0	2016	10.82	34.404	—	—	34.404
A. Lahr	35.000	2011	6.48	—	—	—	35.000
	30.000	2009	9.40		30.000	—	0
	35.000	2009	11.55	—	—	—	35.000
	100.000	2011	20.25	—	—	—	100.000
	125.000	2013	12.23	—	—	—	125.000
	0	2016	10.82	34.802	—	—	34.802
Totals	**2,730,000**			**168,909**	**450,000**	**0**	**2,448,909**

Exercising of options; purchase of shares 2009

On 18 February 2009, 250,000 options with an exercise price of € 9.40 were exercised by Ronald Brus and 85,000 shares were purchased. In addition, 85,000 options with an exercise price of € 9.40 were exercised by Jaap Goudsmit and 10,000 shares were purchased. These exercises were due to the expiration of the options. There were no other exercises of share options held by members of the Management Board.

Shares held by members Management Board and other members of the Management Committee

The Management Board members held the following shares in the Company at 30 June 2009:

Name of holder	Ordinary shares held on 30 June 2009	% of total ordinary shares on 30 June 2009	Ordinary shares held on 31 December 2008	% of total ordinary shares on 31 December 2008
R.H.P Brus	239,202	0.36%	154,202	0.23%
L. Kruimer	28,195	0.04%	28,195	0.04%
C. de Jong	2,406	0.01%	2,406	0.01%
J. Goudsmit	169,276	0.25%	159,276	0.24%
R. Beukema	41,282	0.06%	22,582	0.03%
A. Lahr	9,789	0.01%	9,789	0.01%
Total	**439,079**	**0.66%**	**344,079**	**0.52%**

As of 30 June 2009, 66,561,032 Shares were issued. As of 31 December 2008, 65,833,242 Shares were issued.

Options held by members Supervisory Board

The Supervisory Board members held the following options during the period ended 30 June 2009:

Name of Holder	Options held at 31 December 2008	Exercised Jan – Jun 2009	Options held at 30 June 2009
J.P. Oosterveld	10,000	—	10,000 (1)
	10,000	—	10,000
S.P. Lance	10,000	—	10,000
	10,000	—	10,000
P.M. Satow	10,000	—	10,000
	22,000	—	22,000
	10,000	—	10,000
C.E. Wilhelmsson	10,000	—	10,000
	10,000	—	10,000
A.Hoevenaars	5,000	—	5,000 (2)
	10,000	—	10,000
F. Waller	0	—	0
Totals	**117,000**	**—**	**117,000**

(1) J.P. Oosterveld exercised these 10,000 options on 8 October 2009 in exchange for cash.

(2) A. Hoevenaars exercised these 5,000 options on 8 October 2009 in exchange for cash.

Shares held by members Supervisory Board

The Supervisory Board members held the following shares in the Company during the period ended 30 June 2009:

Name of holder	Shares held at 30 June 2009 [1]	% of total Shares	Shares held at 31 December 2008	% of total Shares
J.P. Oosterveld	12,000	0.02%	9,500	0.01%
A. Hoevenaars	10,000	0.02%	7,500	0.01%
S.P. Lance	12,500	0.02%	—	—
P.M. Satow	66,300 [2]	0.10%	63,800	0.10%
C.E. Wilhelmsson	10,000	0.02%	7,500	0.01%
S. Davis	5,000	0.00%	—	—
F. Waller	—	0.00%	—	—
Total	**115,800**	**0.17%**	**88,300**	**0.13%**

(1) On 5 February 2009, a total of 27,500 shares were granted to members of the Supervisory Board.

(2) Mr. P.M. Satow acquired and additional 7,010 of our ADSs in the open market on 1 October 2009.

As of 30 June 2009, 66,561,032 Shares were issued. As of 31 December 2008, 65,833,242 Shares were issued.

11.6 Other information

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 salary for the Management Board members. No such severance arrangements have been entered into with members of the Supervisory Board.

None of the members of the Management Board or any other member of the Management Committee and he Supervisory Board is, or has been, subject to (i) any convictions in relation to fraudulent offences in the last five years, (ii) any bankruptcies, receiverships or liquidations of any entities in which such members held any office, directorships or senior management positions in the last five years, or (iii) any official public incrimination and/or sanctions of such person by statutory or regulatory authorities (including designated professional bodies), or disqualification by a court from acting as a member of the administrative, management or supervisory bodies of an Issuer or from acting in the management or conduct of the affairs of any Issuer for at least the previous five years.

11.7 Employees

As of 30 June 2009, we had 1,168 employees. The average number of employees in 2008 was 1,142. Personnel as at 30 June 2009 were employed in the following categories:

	30 June 2009	2008	2007	2006
Research and Development	312	303	368	381
General and administrative	151	147	134	125
Operations	543	527	466	452
Marketing and sales	162	149	158	115
Total	**1,168**	**1,126**	**1,126**	**1,073**

The Group's personnel are located primarily in the Netherlands, Switzerland, Spain, Italy, South Korea, Sweden, the US and China.

The split per geographical area is as follows:

	30 June 2009	2008	2007	2006
Europe	895	861	915	902
North America	20	19	19	17
Asia	253	246	192	154
Total	**1,168**	**1,126**	**1,126**	**1,073**

11.8 Equity-based incentives to employees

The Group maintains stock option plans whereby the Remuneration committee of the Supervisory Board may grant options to employees, members of the Management Board and members of the Supervisory Board. The compensation expenses included in operating expenses for those plans were € 5.1 million, € 6.6 million and € 4 million in 2008, 2007 and 2006, respectively.

In December 2004, the Supervisory Board approved a new option plan providing the grant of stock options to employees. 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 the date of grant. Upon termination of employment with Crucell, 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 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.

At the annual General Meeting in 2008, the Shareholders approved the revised long-term incentive (**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 fulfilment of the LTI performance condition. On the vesting date, our TSR performance is measured against the performance of the NASDAQ Biotechnology Index during the performance period. The positive difference in percentages, if any, between our 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 new LTI plan will impact the Group's results for the first time in 2009.

At the annual General Meeting in 2008, the Shareholders 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 which started 2 June 2008. The conditionally granted options include a market condition that is taken into account when estimating the fair value of the options granted. The market condition is an absolute total shareholder return of at least 50% of the share value measured three years after the date of the grant.

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:

In percentages	Period ended on 30 June 2009	Year ended 31 December 2008	Year ended 31 December 2007	Year ended 31 December 2006
Risk-free interest rate	2.4%	4.3%	4.1%	3.6%
Expected dividend yield	-	-	-	-
Expected volatility	50.9%	36.7%	33.3%	41.8%
Expected life (years)	4.40	4.76	4.25	4.25

The risk-free interest rate is based on Dutch treasury securities applicable at the time of grant. In determining the expected volatility, we take into account the historical volatility of the Company's stock over a period commensurate with the expected term of the employee stock options. When establishing the expected life, we take into account the contractual term of the options and historical employee exercise behaviour. The weighted average fair value of options granted during the years ended 31 December 2008, 2007 and 2006 was € 4.03, € 5.34 and € 6.96, respectively. The weighted average fair value of options granted during the first half year of 2009 was 6,37.

A summary of the stock option activity for the outstanding plans is as follows:

	Number of options	Weighted average exercise price
Balance at 1 January 2006	**4,029,504**	**6.43**
Granted	953,466	18.76
Exercised	(1,284,655)	4.16
Forfeited	(12,875)	19.40
Balance at 31 December 2006	**3,685,440**	**10.36**
Granted	1,514,165	16.97
Exercised	(301,475)	6.45
Forfeited	(237,447)	19.15
Balance at 31 December 2007	**4,660,683**	**12.31**
Granted	2,639,640	11.59
Exercised	(420,270)	7.58
Forfeited	(592,175)	16.55
Balance at 31 December 2008	**6,287,878**	**11.92**
Granted	1,086,986	14.33
Exercised	(700,290)	9.24
Forfeited	(125,147)	15.99
Balance at 30 June 2009	**6,549,427**	**12.53**

Also included in the options outstanding as of 31 December 2008 were also options to acquire ordinary shares held by certain former employees and consultants. These individuals have been permitted to continue to hold these options for services rendered.

The following table summarises information about the Company's stock options outstanding at 31 December 2008 and 30 June 2009:

Exercise price in euro	Outstanding options at 30 June 2009	Weighted average exercise price	Weighted average remaining contractual life (years)	Exercisable options	Weighted average exercise price-exercisable options
2.35 - 4.99	511,425	3.34	1.62	511,425	3.34
5.00 - 9.99	998,959	7.53	2.83	663,369	6.60
10.00 - 14.99	3,626,696	12.92	4.19	452,750	12.44
15.00 - 19.99	1,210,516	18.06	2.59	651,463	18.15
20.00 - 22.22	201,831	20.42	1.69	151,411	20.42
Total	**6,549,427**	**12.53**	**3.41**	**2,430,418**	**10.96**

Exercise price	Outstanding options at 31 December 2008	Weighted average exercise price	Weighted average remaining contractual life (years)	Exercisable options	Weighted average exercise price-exercisable options
2.35 – 4.99	516,125	3.34	2.12	516,125	3.34
5.00 - 9.99	1,689,724	8.19	2.22	1,223,104	7.74
10.00 - 14.99	2,677,125	12.45	4.34	247,625	12.74
15.00 - 19.99	1,193,031	18.20	2.92	452,483	17.91
20.00 - 22.22	211,873	20.42	2.19	113,970	20.50
Total	**6,287,878**	**11.92**	**3.24**	**2,553,307**	**9.71**

As of 31 December 2008, a total of 9,874,986 ordinary shares, representing 15% (2007: 15%) of the issued share capital, was reserved for issuance under the option plan, of which 6,287,878 (2007: 4,660,683) were subject to outstanding options.

Share-based incentive plans

In addition to the employee stock option plans for executives as described in the previous paragraph, the Company operated incentive plans for executives up to 2008 that involved the issuance of share awards.

Up to 2008, the Group operated the 2005 Short-term Incentive Plan (the **2005 STI Plan**). We granted executives share awards with vesting contingent upon meeting various company-wide, departmental and individual performance goals. The employees granted shares under the STI Plan were allowed to elect to receive either cash (at a 25% discount from the total award) or shares if certain performance criteria were met.

Grants under the STI Plan were accounted for as liabilities and included in accrued compensation and related benefits in the accompanying balance sheets. In 2007, executives were entitled to a total of 15,544 STI Plan shares, after deduction of income tax. Shares granted under the STI Plan were issued to the executives in the first quarter of 2008. No more issuances under this STI plan can take place. At the annual General Meeting in 2008, the Shareholders approved the 2008 STI cash-based payment plan and this supersedes the 2005 STI share-based payment plan.

Up to 2008, the Group operated the 2005 Long-term Incentive Plan (the **2005 LTI Plan**), which allowed for the issuance of up to 36,842 shares of common stock to be granted to executives with vesting

contingent upon meeting various performance conditions. 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 Shares originally allowed for issuance. In 2008, a total of 20,104 Shares was granted under the terms of the 2005 LTI Plan. No more issuances under this 2005 LTI Plan can take place. At the annual General Meeting in 2008, the Shareholders approved the 2008 LTI option-based payment plan as described above and this supersedes the 2005 LTI share-based payment plan.

11.9 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 present value of the defined benefit obligation at the balance sheet date, less the fair value of the plan assets after adding or subtracting unrecognized actuarial gains or losses and 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 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 net actuarial losses and 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. Actuarial gains and losses in excess of a threshold of the higher of 10% of the pension liabilities and 10% of the fair value of the plan assets are charged or credited to the income statement over the employees' expected average remaining working lives.

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.

Recognition of pension expenses in the income statement and balance sheet (in thousands of euro):

	Year ended 31 December		
Income statement	**2008**	**2007**	**2006**
Defined benefit plans	(139)	(1,592)	1,712
Defined contribution plans	2,408	2,436	1,770
Total	**2,269**	**844**	**3,482**

	Year ended 31 December	
Balance sheet	**2008**	**2007**
Defined benefit plans		
Pension assets	8,612	7,397
Pension liabilities	(2,710)	(3,466)
Net pension asset	5,902	3,931

Prior to the acquisition of Berna Biotech and SBL, the Group did not operate any defined benefit plans. Since the acquisitions in 2006, the Group operates defined benefit plans in Switzerland, South Korea and Sweden. The pension asset of € 8.6 million (2007: € 7.4 million) relates to the Swiss pension fund while, the pension liability of € 2.7 million (2008: € 3.5 million) relates to the Swedish and the South Korean pension funds. In total, 97% (2007: 96%) of the plan assets and 91% (2007: 90%) of the defined benefit obligation relate to the Swiss pension fund. For further details we refer to note 5.10 to the 2008 Financial Statements.

12 MAJOR SHAREHOLDERS

The following table sets out the name of each person other than a member of our Management Board or the Supervisory Board[1] who, as at the date of this Prospectus and as far as we are aware of, has a direct or indirect interest in our share capital, which interest is to be disclosed under Dutch law. The information derives from the register of the Financial Supervision Act maintained by the AFM as per the date of this Prospectus.

Shares				
Name	**% of share capital**	**Capital and voting interest**	**Manner of disposal**	**Number of voting rights and Shares**
Johnson & Johnson	18%	Real	Indirectly through JHC Nederland B.V.	14,626,984
A. van Herk	8.6%	Real	Indirectly through Onroerend Goed Beheer en Beleggingsmaat-schappij A. van Herk B.V.	6,986,185
Aviva plc (1)	5.92%	Real	Indirectly though Delta Lloyd Levensverzekering N.V., Delta Lloyd Schadeverzekering N.V. and Delta Lloyd Nederland Fonds N.V.	3,514,130

(1) According to latest filing on 1 November 2006.

Except as disclosed above, we are not aware of any person who, as of the date of this Prospectus, directly or indirectly, has a beneficial interest in 5% or more of our Shares. Our major shareholders have the same voting rights as the other holders of the Shares.

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.

Equity Purchase Agreement, Shareholder Agreement and Collaboration Agreements

On 28 September 2009, we and Investor entered into an equity purchase agreement (the **Equity Purchase Agreement**), a registration rights agreement (the **Registration Rights Agreement**), the Shareholder Agreement and the Collaboration Agreements.

Pursuant to the Equity Purchase Agreement Investor acquired the New Shares against the Issue Price. The Issuance has resulted in a dilution to our Shareholders' (other than Investor) proportionate ownership and voting interest in the Company of approximately 18%. The Equity Purchase Agreement contains customary representations and warranties. Pursuant to the registration rights agreement Investor was granted certain customary rights regarding the registration of the New Shares under the US Securities Exchange Act 1934, as amended.

For further details on the Collaboration Agreements, see Chapter 10 "Business Overview".

[1] Some members of our Management Board and Supervisory Board own Shares and options to acquire Shares. We describe their Share and option holdings in more detail in Chapter 11 "Management Board, Supervisory Board and Employees".

The following is a summary of certain important elements of the Shareholder Agreement.

- Lock-Up

For a period of three months following the Issue Date, the Investor shall not be permitted to, directly or indirectly, dispose of all or part of the New Shares (or ADSs acquired in exchange for New Shares). Customary exceptions apply to the lock-up.

The lock-up period will terminate immediately in the event that a third party publicly announces a public offer or acquires 18% or more of the Shares (including Shares represented by ADSs), in each case, without the consent or recommendation of the Management Board or Supervisory Board, the Company intends to enter into or announces publicly that it is considering a transaction involving the acquisition by a third party of more than 30% of our shares or assets, or the Collaboration Agreements are terminated (other than as a result of a material breach by Investor).

- Standstill

For a period of three years from the Issue Date, the Investor and its affiliates may not, without our prior approval, purchase or acquire any Shares or securities convertible into, or exercisable or exchangeable for, or otherwise giving the holder thereof any rights in respect of, Shares (including Shares represented by ADSs) or commence a public offer for our Shares, if, in either case, the consummation of such purchase or acquisition or public offer would result in the Investor 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 (including Shares represented by ADSs). Customary exceptions apply to the standstill.

- Anti-Dilution

If, within nine months from the Issue Date, we experience the consummation of a negotiated transaction for a change of control of Crucell at a price per share below the Issue Price Investor 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 Investor on the Issue Date).

This amount must be paid to Investor 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 us.

- Drag Along Right

If we receive a bona fide public offer from a third party and (i) our 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 (including Shares represented by ADSs) (including those held by Investor and/or its Affiliates) have tendered their shares to the third party in connection with such public offer and (iii) the Investor and/or any of its Affiliates do not have a bona fide matching (x) counter public offer to our Shareholders or (y) other proposal to us involving the acquisition by a third party of more than 30% of our shares or assets pending, the Investor and its affiliates shall agree to tender and sell all their Shares in such public offer. Investor shall in such event, if applicable, also have the right to receive payment of the amount as described under “Anti-Dilution Right Investor” in the preceding paragraph.

- Pre-Emptive Right

If we at any time propose 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 (including Shares represented by ADSs), Investor 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 ESOP) (subject to customary exceptions). The Investor's pre-emptive right shall expire and no longer be available upon the Investor (together with its affiliates) ceasing to beneficially own at least 12% of our issued and outstanding Shares (including Shares represented by ADSs).

- Approval Rights

We may not without the approval of the Investor: (i) commence a tender offer or repurchase of Shares if the consummation of such tender offer or repurchase would result in the Investor holding more than 18% of the issued and outstanding Shares (including Shares represented by ADSs), (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. The Investor's approval right shall expire and no longer be available upon the Investor (together with its affiliates) ceasing to beneficially own at least 10% of our issued and outstanding Shares (including Shares represented by ADSs).

13 RELATED PARTY TRANSACTIONS

13.1 Related party transactions within the Group

We have related party transactions and balances with joint venture partners, Investor, associates and directors and executive officers. We conduct related party transactions at arm's length and subject to terms comparable to market conditions. There are no related party transactions outside the normal course of business.

The following table provides the total value of transactions which have been entered into with related parties, excluding directors and executive officers, for the relevant financial year.

In thousands of euro	Income and expenses for the year ended 31 December			Balance outstanding as at 31 December	
Related party	**2008**	2007	2006	**2008**	2007
Sales of goods and services					
Pevion Biotech AG	**-**	364	251	**-**	**-**
Kenta Biotech AG	**130**	223	168	**-**	**-**
ADImmune Corp.	**3,262**	2,271	**-**	**4,495**	6,724
Expenses					
Percivia	**(4,081)**	(4,247)	(1,227)	**(1,023)**	(332)
Avv Falaguerra	**(34)**	(17)	(12)	**(43)**	(6)
Kenta Biotech AG	**-**	**-**	(60)	**-**	**-**

Mr. Falaguerra, the chairman of the executive board of our Italian subsidiary Berna Biotech Italia Srl, is related to Avv. Falaguerra, an Italian firm that provided taxation services to the Italian subsidiary. This arrangement has been discontinued.

In addition to the information contained in the table above we have entered into transactions with (affiliates of) Investor in the ordinary course of business.

13.2 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 period ended on 30 June 2009, the Group did not make any provision for doubtful debts relating to amounts owed by related parties (31 December 2008: nil). This assessment is undertaken each financial year through examining the financial position of the related party and the market in which the related party operates.

13.3 Transactions with members of the Management Board, Supervisory Board and employees

We have no knowledge of any transactions with our Management Board members, Supervisory Board members and senior management, with the exception of the arrangements made regarding their remuneration (reference is made to Chapter 11.4 "Management Board, Supervisory Board and Employees – Remuneration") and with the exception of the loans to the members of the Management Board and senior management as set out hereunder.

The following table describes loans that have been granted to the members of our Management Board and senior management since 1 January 2001. We have not granted any loans to any Supervisory Board member. We set 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 our Shares. These loans become payable at the time Shares received on exercise of the related options are sold or immediately if the employee ceases to work for us before this time. We fund payments due under loans granted prior to 30 July 2002, the date legislation was passed in the US prohibiting the granting of additional loans to company officers.

Amounts in thousand euro	Largest amount of loan outstanding since 1 January 2001	Amount of loan outstanding at 31 December 2008	2008 interest rate in %
Name			
R.H.P. Brus	132	87	3.5%
J. Goudsmit	25	-	3.5%
Other Personnel	61	47	3.5%
		134	

13.4 Transaction with Investor

We entered into the Equity Purchase Agreement, the Shareholder Agreement, the Registration Rights Agreement and the Collaboration Agreements with Investor (or its affiliates). See for further details on the Shareholder Agreement Chapter 12 “Major Shareholders” and for further details on the Collaboration Agreements Chapter 10 “Business Overview”.

14 SHARE CAPITAL AND CORPORATE GOVERNANCE

Set out below is a summary of some relevant information concerning the Shares and a brief summary of certain provisions of Dutch corporate law and the Articles of Association.

This summary does not purport to be complete and is qualified in its entirety by reference to, and should be read in conjunction with, the Articles of Association or with Dutch law, as the case may be. The full text of the Articles of Association is incorporated in this Prospectus by reference and is available, in Dutch and in English, at the Company's head office and on the Company's website (reference is also made to paragraph 16.1 "General Information – Available information").

14.1 General

We are a public limited liability company (*naamloze vennootschap*) under Dutch law, with our statutory seat in Leiden, the Netherlands, with the legal and commercial name Crucell N.V., registered with the Chamber of Commerce in The Hague, the Netherlands, under number 28087740. We were incorporated on 9 October 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. The most recent change to the Articles of Association is dated 12 June 2009. 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 Group. The Company has subsidiaries in the Netherlands, Switzerland, Spain, Italy, Sweden, South Korea, the United Kingdom and the US.

14.2 Corporate objects

The objects of the Company are set out in article 3 of the Articles of Association. Our objects include acquiring, establishing, managing and cooperating with 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.

14.3 Composition of share capital

Authorized and issued share capital

Our authorized share capital amounts to € 75 million divided into: 156,250,000 Shares and 156,250,000 preference shares, each with a par value of € 0.24.

Set out below are the amounts of outstanding shares and the authorized share capital in 2006, 2007 and 2008 and 30 June 2009.

	Authorized ordinary share capital		Ordinary shares issued and fully paid	
	Ordinary shares	Authorized capital €	Ordinary shares	Issued capital €
At January 1, 2006	**85,000,000 (1)**	**20,400,000**	**41,440,613**	**9,945,747**
Issued in February 2006 in exchange for issued share capital of Berna Biotech	-	-	16,930,761	4,063,383
Shares issued in relating to private placement and acquisition of minority interests			5,022,627	1,205,430
Shares issued relating to share-based payments	-	-	1,408,324	337,998
At December 31, 2006	**85,000,000**	**20,400,000**	**64,802,325**	**15,552,558**
Shares issued relating to share-based payments	-	-	547,471	130,913
At December 31, 2007	**85,000,000**	**20,400,000**	**65,347,796**	**15,683,471**
Shares issued relating to share-based payments	-	-	484,446	116,507
At December 31, 2008	**85,000,000**	**20,400,000**	**65,833,242**	**15,799,978**
Shares issued relating to share-based payments	-	-	727,790	174,665
At June 30, 2009	**156,250,000 (2)**	**37,500,000**	**66,561,032**	**15,974,643**

(1) Authorized capital pursuant to an amendment of the Company's articles of association on 21 October 2004.

(2) Authorized capital pursuant to an amendment of the Company's articles of association on 12 June 2009.

The authorised preference share capital as per 1 January 2006, 31 December 2006, 31 December 2007, 31 December 2008 and 30 June 2009 is equal to the authorised ordinary share capital. Since our incorporation no preference shares have been issued.

Form and trading of Shares

The Shares can be issued in bearer or registered form and will be in bearer form unless the Shareholder indicates otherwise in writing. The preference shares can only be issued in registered form. No share certificates will be issued for shares in registered form.

Our Shares (other than the New Shares) are admitted to trading on Euronext Amsterdam. We seek admission to trading of the New Shares and we have prepared this Prospectus to that purpose. If the Listing succeeds, all the New Shares will be traded on Euronext Amsterdam.

All of our bearer Shares are embodied in a single global share certificate which will not be exchanged for single or multiple physical securities and which is deposited in a giro deposit (*girodepot*) with the Dutch Securities Depository (Euroclear Nederland) and collective deposits (*verzameldepots*) of financial institutions admitted to Euroclear Nederland for safekeeping on behalf of the parties entitled to the Shares in bearer form, in accordance with the Securities (Bank Giro Transactions) Act (*Wet giraal effectenverkeer*). The Shares represented by the single global share certificate may only be transferred through the book-entry system (*giro*) maintained by Euroclear Nederland. A participant in the collective deposit of a financial institution admitted to Euroclear Nederland may, at his own expense, require conversion of one or more of his bearer Shares into Shares in registered form. Application has been made for the New Shares to be accepted for delivery through the book-entry facilities of Euroclear Nederland. Euroclear Nederland is located at Herengracht 459-469, 1017 BS Amsterdam, the Netherlands.

We enter holders of registered 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 Shares registered in his name. We are required to provide this free of charge. Dutch law requires that transfers

of registered 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.

The Shares are also traded on SWX Swiss Exchange.

Part of the Shares are also 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.

Outstanding options

There are 6,641,142 options outstanding as per 30 September 2009..

Issue of Shares and pre-emptive rights

Our General Meeting, or our Management Board if the General Meeting has delegated the power to it, has the authority to decide on any issuance of Shares or rights to subscribe for Shares and on the terms and conditions of such issuance. The General Meeting has delegated the power to issue Shares to the Management Board until 30 November 2010, and the authorization may at any time be extended by the General Meeting for a period of up to five years. Our Management Board's authority to issue Shares is limited to a maximum of 15% of the issued share capital at the time of issue, plus a further issue of up to 15% of the issued share capital at the time of issue if the issue takes place in relation to a merger, a cooperation or an acquisition. A resolution by the Management Board to issue shares is subject to approval by the Supervisory Board.

The above applies by analogy to the granting of rights to subscribe for Shares but is not applicable to the issue of Shares to persons exercising a previously granted right to subscribe for Shares.

Without prior specific authorization from our General Meeting our Management Board may not issue preference shares or grant options for such shares if, as a result, more preference shares than Shares will or could become outstanding.

Each holder of Shares has pre-emptive rights to subscribe for any Shares that we issue and has pre-emptive rights to subscribe if we grant rights to subscribe for Shares. Pre-emptive rights are in proportion to the percentage of our outstanding Shares that the holder owns. Pre-emptive rights do not apply to Shares issued for a non-cash contribution, to Shares issued to our employees or Shares issued to a person who exercises a previously acquired right to subscribe for Shares. Holders of preference shares do not have pre-emptive rights if we issue Shares, and holders of Shares have no pre-emptive rights to purchase preference shares if we issue preference shares.

If our Management Board has been delegated the power to issue shares, it can limit or exclude any pre-emptive rights subject to approval by the Supervisory Board. At present, our Management Board is authorized to issue shares and therewith to limit or exclude any pre-emptive rights. This authorization is valid until 30 November 2010 and the General Meeting may at any time extend this authorization for a period of up to five years.

Under the Shareholder Agreement Investor was granted certain pre-emptive rights. For further details, see Chapter 12 "Major Shareholders".

Our shares cannot be issued below par value. The 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 value must be paid up upon issue, 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 call for payment of the remaining unpaid nominal value (if any) on preference shares.

Acquisition of shares in our capital

We may acquire our own fully paid-up shares if the following conditions are met:

- our General Meeting 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 a price range must be set; and
- 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.

The authorization by the General Meeting to acquire Shares may not exceed a term of 18 months. Currently, the General Meeting has authorized the Management Board to acquire Shares up to 10% of the outstanding share capital of the Company for an 18-month period up to and including 30 November 2010, against a repurchase price between, on the one hand, the nominal value of the shares concerned and, on the other hand, an amount equal to 110% of the highest price officially quoted on the Nasdaq National Market and Euronext Amsterdam on any of five banking days preceding the date of the repurchase.

Furthermore, the General Meeting has authorized the Management Board to repurchase preference shares for a price equal to the nominal value plus accrued interest, if any.

We and our subsidiaries may not vote on 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.

We hold 30,684 Shares in treasury.

Reduction of share capital

If our Management Board proposes, our Supervisory Board approves and Dutch law permits, the General Meeting can reduce our issued share capital by cancellation of shares or reduction of the nominal value of shares.

14.4 Dividends and other distributions

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 pay dividends on issued and outstanding preference shares (if any). With Supervisory Board approval, our Management Board then decides whether and how much of the remaining profit will be allocated to the reserves. Any profits remaining shall be paid as a dividend on the Shares.

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 out of one or more of our reserves.

All distributions on Shares, either as an (interim) dividend or otherwise have to be made in such a way that on each ordinary share an equal amount or value is paid.

14.5 Stichting Preferente Aandelen Crucell

On 25 October 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 our identity, 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 attached 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 Shares outstanding at the time of an acquisition.

Unless the preference shares have been issued by a vote of the General Meeting, our Articles of Association require that a General Meeting be held no later than two years after the issue of preference shares to consider their redemption or cancellation. If the General Meeting does not resolve to redeem or cancel the preference shares, another General Meeting will be held within two years. Until the preference shares have been redeemed or cancelled, a General Meeting to consider a redemption or cancellation of the preference shares will be held within two years of the previous meeting.

In the event of an issue of preference shares pursuant to a resolution of a company body other than the General Meeting as a result of which an amount of preference shares would be issued which would not exceed 100% of the amount of issued Shares, a General Meeting shall be convened and held within four weeks of the issue in which the reasons for the issue shall be explained.

The Preferred Foundation must pay up 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. 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. Jan Oosterveld, in his capacity as chairman of our Supervisory Board, and Pieter Bouw, Mick den Boogert, Sweder van Wijnbergen and Gerard Krans, have been appointed to the board of governors. Pieter Strijkert, former chairman of the Supervisory Board, is an adviser to the board of governors.

Membership of the board of governors of the Preferred Foundation terminates upon:

- voluntary retirement, reaching the age of 72 years, 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 governors 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, provided however, that these members may be reappointed.

14.6 General Meeting and voting rights

We must hold annual General Meetings within six months of the end of our financial year. The annual General Meeting is held, among other things, to adopt our annual accounts. We must hold extraordinary General Meetings of shareholders whenever:

- shareholders and holders of ADSs representing Shares together representing at least one-tenth of our outstanding share capital request a General Meeting 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.

Notice of the General Meeting is given no later than on the fifteenth day prior to the date of the General Meeting. The notice of the meeting states the subjects to be dealt with. 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 shall be authorized to determine a record date to establish which shareholders are entitled to attend and vote in the General Meeting. Such record date may not be set for a date prior to the seventh day before that of the General Meeting. The Management Board must be notified in writing of a registered shareholder's intention to attend the General Meeting.

Shareholders representing alone, or in aggregate, at least 1% of our issued capital or – according to the Euronext Official Price List – at least a value of € 50 million, have the right to request the Management Board and the Supervisory Board to place items on the agenda of the General Meeting. These requests shall be honoured on condition that:

- 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 of the Company 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.

Resolutions are passed by absolute majority of votes cast unless stated otherwise in Dutch law and our Articles of Association.

Dutch law and our Articles of Association do not impose any limitations on non-Dutch ownership or voting of our Shares.

14.7 Amendment of our Articles of Association, merger and demerger and dissolution and liquidation

The General Meeting may only resolve to amend our Articles of Association or to merge or demerge or dissolve us on the proposal of our Supervisory Board.

If the rights of a class of shareholders is affected by an amendment to the Articles of Association, this class must approve the amendment.

Under the Shareholder Agreement the Investor was granted certain approval rights in relation to amendments or our Articles of Association. For further details, see Chapter 12 "Major Shareholders".

In the event of dissolution or liquidation, the Management Board will be the liquidators and the Supervisory Board will supervise the liquidation. After all debts and liquidation expenses of the Company have been paid, the holders of preference shares (if any) have first rights to payment of any dividends not fully paid to them in previous years and payment of the nominal value of their preference shares. Any remaining assets will be distributed to the holders of Shares.

14.8 Ranking holders of shares

The rights of holders of the New Shares and our existing Shares will rank *pari passu* with each other.

Under the Shareholder Agreement the investor was granted additional rights. For further details, please see Chapter 12 "Major Shareholders".

14.9 Dutch Corporate Governance Code

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 by the company with the principles and best practice provisions of the Code relating to the Management Board and Supervisory Board. If a company does not, or does not intend to, comply with one or more of the principles and best practice provisions, it must provide 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.

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 General Meeting with respect to control of the functioning of the Management Board and the Supervisory Board, as well as with respect to the 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;
- 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.

In 2003, we 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. The Code of Conduct stresses that one of our most valuable assets is our integrity. The Code of Conduct was amended in 2008 and has been filed as an exhibit to our 2008 Financial Statements. The amended Code of Conduct adheres to the same underlying principles as the original Code of Conduct, but reflects the fact that we are a fully integrated company that operates in numerous countries. No waivers of the Code of Conduct were granted during 2008.

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.

In June 2005, the General Meeting approved our current corporate governance structure. Except for the three provisions of the Corporate Governance Code referred to below, the Company 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. We comply with all of the principles and best practice provisions of the Code, except for the following:

- Remuneration of Management Board members: 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 agreements 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 if otherwise this would obstruct the recruitment of the right person for a Management Board position.

- Loans to the Company's management: 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 Chapter 13 "Related Party Transactions". We have not granted additional loans to Management Board members since 2002.

- Remuneration of Supervisory Board members: We do not apply the provision that remuneration of the members of the Supervisory Board should not include share grants. We deem 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.

14.10 Management Board and Supervisory Board indemnity

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 and Supervisory Board members are released from liability for the exercise of their duties as board members, if our General Meeting 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 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 for liability (i) any breach of such individual's duty of loyalty to the Company or its shareholders, (ii) acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (iii) any transaction from which the member derived an improper personal benefit or (iv) 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 wilful misconduct in the performance of his duties to us, unless the court in which the action was brought determines that indemnification is appropriate nonetheless.

14.11 Notification of holdings of voting rights and capital interest

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 promptly 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 amount of issued and outstanding share capital or voting rights. Such notification is to be made to the AFM no later than the fourth trading day after the AFM has published the Company's notification regarding the change of share capital.

We are 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 promptly notify the AFM of any change in the number of 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 result in 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 Shares.

14.12 Obligations of shareholders to make a public offer

Pursuant to the Financial Supervision Act, a party – whether acting alone or in concert – that acquires predominant control over us has to make a public takeover bid for all the Shares. A party is deemed to have acquired 'predominant control', if it has acquired 30% or more of the voting rights in the General Meeting of the Company.

14.13 Squeeze-out procedures

If a person or company or group company holds a total of at least 95% of a company's issued share capital by nominal value for its own account (the **Controlling Entity**), Dutch law permits the Controlling Entity to acquire the remaining shares in the company by initiating squeeze-out proceedings against the holders of the remaining shares. The price to be paid for such shares will be determined by the Enterprise Chamber.

Minority shareholders that have not tendered their shares under a public offer have the right to sell their shares to a Controlling Entity, if such Controlling Entity has acquired at least 95% of the class of shares subject to a public offer and represents at least 95% of the total voting rights attached to these shares.

14.14 Market abuse regime

We are required to make inside information, as defined in the Financial Supervision Act, public. We must also provide the AFM with this inside information at the time of publication. Furthermore, we must without delay publish the inside information on our website and keep it available on our website for at least one year.

Company insiders, as described in the Financial Supervision Act, are obliged to notify the AFM when they carry out or cause to be carried out, for their own account, a transaction in Shares or in securities of which the value is at least in part determined by the value of such Shares.

Company insiders include (i) members of the Management Board, (ii) Members of the Supervisory Board and (iii) persons who have a managerial position within the company and in that capacity are authorised to make decisions which have consequences for the future development and prospects of the company and can have access to inside information on a regular basis.

In addition, certain persons designated by the Market Abuse Decree who are closely related, such as spouses and children, with the members of the Management Board, the Supervisory Board or any other insider referred to above, must notify the AFM of the existence of any transaction conducted for their own account relating to the Shares or securities of which the value is at least in part determined by the value of such Shares.

This notification must be made no later than the fifth business day following the transaction date. The notification may be delayed until the moment that the value of the transactions performed for that person's own account, together with the transactions carried out by the persons closely associated with that person, reach or exceed an amount of € 5,000 in the calendar year in question.

Non-compliance with the reporting obligations under the Financial Supervision Act could lead to criminal fines, administrative fines, imprisonment or other sanctions. In addition, non-compliance with the reporting obligations under the Financial Supervision Act may lead to civil sanctions.

We have adopted an internal Code of Conduct including a section on insider dealing with respect to the holding of and carrying out of transactions in Shares by the members of our Management Board and Supervisory Board and our employees. Furthermore, we have drawn up a list of those persons working for the Company who could have access to inside information on a regular or incidental basis and we have informed the persons concerned of the rules on insider trading and market manipulation including the sanctions which can be imposed in the event of a violation of those rules. A copy of our insider dealing policy is provided to each (new) employee and can be obtained from the compliance team or found on our intranet site.

15 TAXATION

15.1 Certain Dutch tax consequences for holders of ordinary Shares or ADSs

The following is a summary of the material Dutch 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. Not every potential tax consequence of such investment under the laws of the Netherlands will be addressed. 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.

The summary of certain Dutch taxes set out in this Chapter 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

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 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' (*rendementsgrondslag*) 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.

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 resulting from other activities, as are Dutch Corporate Entities.

Any benefits derived or deemed to be derived from the ordinary Shares or ADSs (including any capital gains realised 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 in his hands. The same applies to a Dutch Individual for whom the benefits derived from the ordinary Shares or ADSs are treated as resulting 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 in its hands.

Withholding tax

Dividends we distribute are generally subject to a withholding tax imposed by the Netherlands at a rate of 15%.We will withhold this tax from the dividends we distribute. The concept 'dividends we distribute' used in this Chapter 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; and

  – 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.

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. A condition to avoid 'dividend stripping' 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 who holds Dutch nationality will be deemed to be resident in the Netherlands if he has been so at any time during the ten years preceding he date of the gift or his death. For purposes of Dutch gift tax, an individual not holding Dutch nationality will be deemed to be resident in the Netherlands if he has been so at any time during the 12 months preceding the date of the gift.

16 GENERAL INFORMATION

16.1 Available information

We were incorporated as a limited liability company (*naamloze vennootschap*) on 9 October 2000 by deed executed before Mr. R.J.J. Lijdsman, civil law notary. The statement of no objection of the Minister of Justice in respect of our deed of incorporation was issued on 9 October 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 12 June 2009 before Mr. R.J.J. Lijdsman, civil law notary.

Copies (in print) of:

- the Articles of Association (in Dutch and English);
- the Audited Financial Statements; and
- the Semi-Annual Financial Statements,

are available and can be obtained free of charge for 12 months from the date of publication of this Prospectus at our head office at Archimedesweg 4, 2333 CN Leiden, the Netherlands, during normal business hours and in electronic form at the Company's website: www.crucell.com.

Copies (in print) of this Prospectus and any supplement to this Prospectus if any may be obtained free of charge for 12 months from the date of publication of this Prospectus by sending a request by e-mail or in writing to us at the following address:

Crucell N.V.

Attn: Mr. Rene Beukema, General Counsel and Corporate Secretary

Archimedesweg 4
2333 CN Leiden

P.O. Box 2048
2301 CA Leiden
The Netherlands

Alternatively, Dutch residents may obtain copies of this Prospectus in electronic form free of charge for the same period through our website (www.crucell.com), or through the website of the AFM.

16.2 Legal proceedings

There are and there have not been any governmental, 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 financial position or profitability nor, as far as we are aware, are any such proceedings pending or threatened.

Berna Biotech AG on 1 September 2009 received service of a claim filed with a Brazilian court in August 1999 by the Brazilian Health Agency (Fundaçao Nacional de Saúde, **FNS**) totalling Reais 728,382 (€ 266,066; pursuant to euro/ Real exchange rate as per 30 June 2009 of 1.73760).The claim relates to an alleged breach of the specifications of 6 million doses of DTP supplied by Berna Biotech AG to FNS in 1996. Crucell retained Brazilian counsel and took appropriate action. Maximum exposure of Berna Biotech AG is currently estimated at Reais 728,382 (€ 266,066).

16.3 Advisers

Allen & Overy LLP acts as our Dutch counsel and Cleary Gottlieb Steen & Hamilton LLP acts as our US counsel, in connection with the Issuance and this Prospectus.

16.4 Independent auditors

Our Audited Financial Statements included by reference in this Prospectus have been audited by Deloitte Accountants B.V., independent auditors, as stated in their reports included by reference herein. The auditor's reports have been unqualified. Our auditors have no commercial interest in us.

Deloitte Accountants B.V. is located at Orlyplein 10, 1043 DP Amsterdam, the Netherlands. The auditors who sign on behalf of Deloitte are members of the Royal Netherlands Institute of Registered Accountants (*Koninklijk Nederlands Instituut van Registeraccountants*).

Our condensed consolidated interim financial information for the six months ended 30 June 2009 and the six months ended 30 June 2008, which have been provided for comparison purposes, have not been audited nor reviewed.

Deloitte Accountants B.V. has given, and has not withdrawn, its consent to the inclusion or incorporation by reference of its reports on the Audited Financial Statements in this Prospectus in the form and context in which they are included.

16.5 Paying Agent

ABN Amro Bank N.V.

17 DEFINITIONS

2005 LTI Plan	means the 2005 Long-term Incentive Plan for employees of the Group
2005 STI Plan	means the 2005 Short-term Incentive Plan for employees of the Group
2006 Financial Statements	means the audited consolidated annual financial statements and the auditor's report for the financial year ended 31 December 2006
2007 Financial Statements	means the audited consolidated annual financial statements and the auditor's report for the financial year ended 31 December 2007
2008 Financial Statements	means the audited consolidated annual financial statements and the auditor's report for the financial year ended 31 December 2008
Ad5	means adenovirus serotype 5
Ad26	means adenovirus serotype 26
ADSs	means American Depository Shares
AERAS	means Aeras Global TB Vaccine Foundation
AFM	means Netherlands Authority for the Financial Markets *(Stichting Autoriteit Financiële Markten)*
AIDS	means acquired immune deficiency syndrome
Articles of Association	means the articles of association of the Company
Audit Committee	means the audit committee of the Company comprising members of the Supervisory Board
Audited Financial Statements	means the 2006 Financial Statements, 2007 Financial Statements and 2008 Financial Statements
Anti-Dilution Period	means the period ending nine months after the Issue Date
ARV	means Antiretroviral drugs
Bank of New York Mellon	means the Bank of New York Mellon Corporation
BCG	means Bacille Calmette-Guérin
BMF	means Biologics Master File
BSL-III	means Biosafety Level III
CDC	means the Center for Disease Control in Georgia, US
CEO	means chief executive officer
CFO	means chief financial officer
Chamber of Commerce	means the Dutch Chamber of Commerce
CHF	means Swiss Franc, the currency of Switzerland
Code of Conduct	means the code of conduct of the Company

Collaboration Agreements	means (i) a flu-mAb collaboration agreement with regard to the discovery, development and commercialization of antibodies against influenza A virus and (ii) an agreement on the innovation, development and commercialization of novel antibodies, vaccines and/or small molecules having pharmaceutical properties useful in preventing, treating and diagnosing various disease indications, limited to a number of targets, entered into between Crucell Holland B.V. and Ortho-McNeil-Janssen Pharmaceuticals, Inc., an Affiliate of Investor, on 28 September 2009 concurrently with and in relation to the Issuance.
Company	means Crucell N.V.
Controlling Entity	means a person, company or group company that holds a total of at least 95% of the aggregate nominal value of a company's issued share capital for its own account
Corporate Governance Code	means the Dutch Corporate Governance Code
CRADA	means collaborative research and development agreement
CRS	means congenital rubella syndrome
Crucell	means Crucell N.V. and, where appropriate, any or all of its subsidiaries.
CSP	means circumsporozoite protein
CTB	means cholera toxin B
DNB	means the Dutch Central Bank *(De Nederlandsche Bank)*
Dutch Corporate Entities	means investment institutions *(beleggingsinstellingen)* and tax exempt investment institutions *(vrijgestelde beleggingsinstellingen)* as defined in the Dutch Corporate Income Tax Act 1969
Dutch Individuals	means 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 Shares or ADSs, excluding individuals who invest in the Shares or ADSs that form part of a substantial interest (as described below) or deemed substantial interest in the Company and excluding individuals who are our employees or who are deemed to be employees of the Company or employees of any entity related to the Company
Dutch Securities Depository	means the Central Securities Depository of Euroclear Nederland
EMEA	means the European Medicines Agency of the European Union
Enterprise Chamber	means the Enterprise Chamber of the Amsterdam Court of Appeal *(Ondernemingskamer van het Gerechtshof te Amsterdam)*
Equity Purchase Agreement	means the equity purchase agreement between the Company and JHC Nederland B.V., dated 28 September 2009
ERIG	means Equine Rabies Immune Globulin
ESOP	means the remuneration policies regarding employee and management options as prepared by the Remuneration Committee, as adopted and amended by the relevant constituencies of the Company from time to time, including any long term and short term incentives plans adopted or implemented in accordance therewith

ETEC	means Enterotoxigenic Escherichia Coli
EU	means European Union
euro or €	means the currency of the Economic and Monetary Union
Euroclear	means Euroclear Bank S.A./N.V. operator of the Euroclear System
Euroclear Nederland	means Nederlands Centraal Instituut voor Giraal Effectenverkeer B.V., the Dutch depository and settlement institute, a subsidiary of Euroclear
Euronext Amsterdam	means Euronext Amsterdam by NYSE Euronext
Euronext Brussels	means Euronext Brussels by NYSE Euronext
Euronext Official Price List	means the latest Euronext Official Price List published by Euronext Amsterdam N.V.
FDA	means the United States Food and Drugs Administration
Financial Supervision Act	means the Dutch Financial Supervision Act *(Wet op het financieel toezicht)* and the rules promulgated thereunder
FNS	Fundaçao Nacional de Saúde (Brazilian Health Agency)
General Meeting	means the General Meeting of shareholders of the Company
Galapagos	means Galapagos B.V.
GMP	WHO Good Manufacturing Practices
Group	means Crucell N.V. and, where appropriate, any or all of its subsidiaries
GSK	means GlaxoSmithKline
H1 2008 Statements	means the unaudited consolidated interim financial statements as at and for the first half year ended 30 June 2008
H1 2009 Statements	means the unaudited consolidated interim financial statements as at and for the first half year ended 30 June 2009
IP	means intellectual property
HAV	means hepatitis A virus
HBV	means hepatitis B virus
HCV	means hepatitis C virus
HRIG	means Human Rabies Immune Globulin
IASB	means the International Accounting Standards Board
IFRS	means International Financial Reporting Standards
Independent Sources	means independent industry publications, government publications, reports by market research firms or other published independent sources
Insider	means any member of the Management Board and the Supervisory Board and any other person who has managerial responsibilities or who has the authority to make decisions affecting Crucell's future developments and business prospects or who has regular access to inside information relating, directly or indirectly, to Crucell

Investor	means JHC Nederland B.V.
Issuance	means the issuance by the Company of the New Shares at a price of € 20.63 each to the Investor on 28 September 2009
Issue Date	means 28 September 2009
Issue Price	means a price of € 20.63 per New Share
Issuer	means a legal entity which issues or proposes to issue securities
South Korea	means the Republic of Korea
KRW or Korean Won	means South Korean Won
Listing Date	means the date on which the trading in the New Shares on Euronext Amsterdam will commence which is on or about 30 October 2009
Market Abuse Decree	means the Dutch Decree on Market Abuse pursuant to the Financial Supervision Act *(Besluit Marktmisbruik Wft)*
Member State	means a member state of the European Economic Area
Management Board	means the management board *(raad van bestuur)* of the Company
Management Committee	means the management committee of the Company
MDCK	means Madin Darby Canine Kidney cells
MDR-TB	means Multidrug-resistant TB
NASDAQ National Market	means the NASDAQ National Market by NASDAQ OMX Group, Inc.
NASDAQ Global Select Market	means NASDAQ Global Select Market by NASDAQ OMX Group, Inc.
NASDAQ rules	means the NASDAQ Listing Rules
New Shares	means the 14,626,984 Shares issued to the Investor on 28 September 2009
NIAID	means National Institute of Allergy and Infectious Diseases
IND	means Investigational New Drug Application
Nomination Committee	means the nomination committee of the Company comprising of members of the Supervisory Board
Noon Buying Rate	means the noon buying rate in New York City for cable transfers in foreign currencies as certified for customs purposes by the Federal Reserve Bank of New York
NVI	means Netherlands Vaccine Institute
Original Market Price	means the average of the daily volume-weighted average price of the Shares listed on Euronext Amsterdam for each of the 35 (thirty-five) consecutive Euronext Amsterdam trading days immediately preceding the Issue Date
PCT	Patent Cooperation Treaty
PEP	means post-exposure prophylaxis
PERCIVIA	means PERCIVIA PER.C6 Development Center in Massachusetts, US, a joint venture between DSM Biologics and Crucell
Prospectus	means this prospectus dated 28 October 2009

Prospectus Directive	means Directive 2003/71/EC of the European Parliament and of the Council of the European Union
R&D	means research and development
Registration Rights Agreement	means the registration rights agreement entered into between the Company and Investor on 28 September 2009
Remuneration Committee	means the remuneration committee of the Company comprising members of the Supervisory Board
SBL	means the Stockholm-based SBL Vaccin Holding AB
Securities	means (i) shares in companies and other securities equivalent to shares in other companies, (ii) bonds and other forms of securitized debt which are negotiable on the capital markets and (iii) any other securities normally dealt in giving the right to acquire any such transferable securities by subscription or exchange or giving rise to a cash settlement excluding those classes of instruments which are normally dealt in on the money market, and having a maturity of less than 12 months
Securities Act	means the United States Securities Act of 1933, as amended
Semi-Annual Financial Statements	means the H1 2008 Statements together with the H1 2009 Statements
Shareholder	means a holder of any of the Shares (including ADSs)
Shareholder Agreement	means the shareholder agreement entered into between the Company and Investor on 28 September 2009
Shares	means ordinary shares in the capital of the Company with a nominal value of 0.24 each
SWX Swiss Exchange	means SIX Swiss Exchange Ltd. by SIX Group
SSI	means Statens Serum Institute Denmark
Stichting Preferente Aandelen or Preferred Foundation	means Stichting Preferente Aandelen Crucell
Supervisory Board	means the supervisory board *(raad van commissarissen)* of the Company
TB	means tuberculosis
TJU	means the Thomas Jefferson University, based in Pennsylvania, US
United States or US	means the United States of America, its territories and possessions, any state of the United States of America and the District of Columbia
US.AMRIID	means US Army Medical Research Institute of Infectious Diseases
US dollar or $	means United States Dollar
US NIH	means US National Institutes of Health
VRC	means Vaccine Research Center
WHO	means the World Health Organization of the United Nations

Company

Crucell N.V.
Archimedesweg 4-6
2333 CN Leiden
The Netherlands

Legal adviser to the Company as to Dutch law

Allen & Overy LLP
Apollolaan 15
1070 AK Amsterdam
The Netherlands

Legal adviser to the Company as to US law

Cleary Gottlieb Steen & Hamilton LLP
City Place House, 55 Basinghall Street
London EC2V 5EH
England

Independent Auditor

Deloitte Accountants B.V.
Orlyplein 10
1043 DP Amsterdam
The Netherlands

Paying Agent

ABN AMRO Bank N.V.
Gustav Mahlerlaan 16
1082 PP Amsterdam
The Netherlands

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