



FORM 20-F

CRUCCELL NV – CRXL

Filed: April 14, 2005 (period: December 31, 2004)

Registration of securities of foreign private issuers pursuant to section 12(b) or (g)

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**UNITED STATES
SECURITIES AND EXCHANGE COMMISSION**
Washington, D.C. 20549

FORM 20-F

Registration statement pursuant to Section 12(b) or 12(g) of the Securities Exchange Act of 1934

OR

Annual Report pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934

For the fiscal year ended: December 31, 2004

OR

Transition Report pursuant to Section 13 or 15(D) of the Securities Exchange Act of 1934

For the transition period from N/A to N/A

Commission file number: 0-30962

Crucell N.V.

(Exact name of Registrant as Specified in its Charter)

Crucell N.V.

(Translation of Registrant's Name into English)

The Netherlands

(Jurisdiction of Incorporation or Organization)

Archimedesweg 4, 2333 CN Leiden, The Netherlands

(Address of Principal Executive Offices)

Securities registered or to be registered pursuant to Section 12(b) of the Act:

None

Securities registered or to be registered pursuant to Section 12(g) of the Act:

Title of each class

Name of each exchange on which registered

**American Depositary Shares,
each representing one Ordinary Share,
par value €0.24**

Nasdaq National Market

Securities for which there is a reporting obligation pursuant to Section 15(d) of the Act:

None

Indicate the number of outstanding shares of each of the issuer's classes of capital or common stock as of the close of the period covered by the annual report:

Ordinary Shares, par value €0.24 36,873,421

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes No

Indicate by check mark which financial statement item the registrant has elected to follow.
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PRESENTATION OF FINANCIAL AND OTHER INFORMATION

Prior to 2000, we published our financial statements in Dutch guilders. We publish our financial statements in euro. In this document, references to (1) "€", "EUR" and "euro" are to the currency introduced at the start of the third stage of the European Economic and Monetary Union pursuant to the Treaty establishing the European Economic Community as amended by the Treaty on European Union, (2) "\$", "USD" and "dollars" are to the currency of the United States and (3) "NLG" and "Dutch guilders" are to the former currency of The Netherlands. We have converted certain amounts in this document, including our historical financial statements, into euro at the rate of EUR 1.00 to NLG 2.20371, the euro/Dutch guilder exchange rate fixed on January 1, 1999.

All amounts set forth in this annual report, unless otherwise noted, are in thousands of euro, except share and option data.

FORWARD-LOOKING STATEMENTS

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

These forward-looking statements involve risks, uncertainties and other factors, some of which are beyond our control, that may cause our results, performance or achievements or conditions in the markets in which we operate to differ from those expressed or implied in these forward-looking statements. We describe certain of these risks and uncertainties in Item 3, "Key Information—Risk Factors." We caution you not to place undue reliance on these forward-looking statements, which reflect our management's view only as of the date of this document.

OTHER

PER.C6®, AdVac® and MAbstract® are trademarks of Crucell Holland B.V., a wholly owned subsidiary of Crucell N.V. Other trademarks of Crucell N.V. or its wholly owned subsidiaries used in this report include Crucell®. All other trademarks, service marks, trade names and registered marks used in this report are trademarks, trade names or registered marks of their respective owners. Crucell N.V. and its wholly owned subsidiaries own a number of additional trademarks, including registered trademarks, that are not referenced in this report.

PART I

Item 1. Identity of Directors, Senior Management and Advisors

This item is not applicable.

Item 2. Offer Statistics and Expected Timetable

This item is not applicable.

Item 3. Key Information

Selected Financial Data

The selected financial data presented below as at and for each of the five years in the period ended December 31, 2004 has been derived from:

- in respect of the three years ended December 31, 2004, our audited financial statements included elsewhere in this annual report, which have been audited by Ernst & Young Accountants, Independent Registered Public Accounting Firm; and
- in respect of the two years ended December 31, 2001, our audited financial statements, which have not been included elsewhere in this annual report, and which have been audited by Ernst & Young Accountants, Independent Registered Public Accounting Firm.

We have prepared our financial statements in accordance with accounting principles generally accepted in the United States (U.S. GAAP). The selected financial data of Crucell N.V. should be read in conjunction with Item 5, "Operating and Financial Review and Prospects" and the audited historical financial statements of Crucell and accompanying notes that are included elsewhere in this annual report.

Years ended December 31,

	2000	2001	2002	2003	2004
(in thousands, except share/ADS and per share/ADS data)					
Consolidated Statements of Operations Data:					
Revenues:					
License	€ 6,045	€ 7,972	€ 6,664	€ 4,800	€ 12,429
Service fees				404	5,712
Government grants and other	865	1,209	2,911	2,220	4,481
Total revenues	€ 6,910	€ 9,181	€ 9,575	€ 7,424	€ 22,622
Costs and expenses:					
Cost of service fees	—	—	—	399	5,644
Research and development	7,189	17,392	24,252	21,885	20,468
Selling, general and administrative	8,218	8,875	10,386	7,606	14,704
Developed technology amortization	665	1,330	1,331	1,330	1,966
Goodwill amortization	4,413	8,826	—	—	—
Goodwill impairment	—	—	30,891	—	—
Stock option compensation	31,153	888	1,371	2,696	2,566
Acquired in-process research and development	84,141	—	—	—	—
Total costs and expenses	€ 135,779	€ 37,311	€ 68,231	€ 33,916	€ 45,348
Loss from operations	(128,869)	(28,130)	(58,656)	(26,492)	(22,726)
Interest income, net	914	6,205	3,547	2,143	1,503
Foreign currency gain/(loss)	(2,219)	463	(54)	(19)	(108)
Equity in losses of unconsolidated investments	(1,443)	(2,524)	(507)	—	—
Gain on sale of available for sale securities	—	—	—	982	—
Net loss	€ (131,617)	€ (23,986)	€ (55,670)	€ (23,386)	€ (21,331)
Net loss per share/ADS—basic and diluted	€ (5.38)	€ (0.68)	€ (1.57)	€ (0.65)	€ (0.59)
Weighted average shares/ADSs outstanding—basic and diluted	24,485,800	35,268,457	35,547,635	35,920,626	36,382,662

As of December 31,

	2000	2001	2002	2003	2004
(in thousands)					

Consolidated Balance Sheet Data:

Assets:					
Cash and cash equivalents	€ 136,056	€ 120,243	€ 110,645	€ 87,210	€ 76,711
Total current assets	€ 138,954	€ 124,861	€ 114,477	€ 100,415	€ 84,155
Intangible assets(1)	€ 45,704	€ 35,548	€ 3,326	€ 1,996	€ 4,047
Total assets	€ 196,525	€ 175,259	€ 129,857	€ 114,406	€ 98,891
Liabilities and shareholders' equity:					
Total current liabilities	€ 9,150	€ 10,546	€ 12,799	€ 11,716	€ 14,773
Total long term liabilities	—	—	€ 5,649	€ 11,045	€ 5,583
Total shareholders' equity	€ 187,375	€ 164,713	€ 111,409	€ 91,645	€ 78,535
Total liabilities and shareholders' equity	€ 196,525	€ 175,259	€ 129,857	€ 114,406	€ 98,891

(1)

Net of accumulated amortization and impairment of €50,752 and €48,786 at December 31, 2004 and 2003, respectively, and accumulated amortization of €47,456 and €15,234 at December 31, 2002 and 2001, respectively.

Exchange Rate Information

The following table sets forth, for the years indicated, the high, low, average and year-end noon buying rates in New York City for cable transfers as certified for customs purposes by the Federal Reserve Bank of New York ("Noon Buying Rates") for euros per USD 1.00.

Year ended December 31,	High	Low	Average(1)	End of Period
	€	€	€	€
2000	1.21	0.97	1.09	1.07
2001	1.20	1.05	1.12	1.12
2002	1.16	0.95	1.06	0.95
2003	0.97	0.80	0.89	0.80
2004	0.85	0.73	0.81	0.73

(1)

The average of the Noon Buying Rates on the last business day of each month during the period indicated.

The following table sets forth, for the previous six months, the high and low Noon Buying Rates expressed in euros per USD 1.00.

	High	Low
	€	€
October 2004	0.82	0.78
November 2004	0.79	0.75
December 2004	0.76	0.73
January 2005	0.77	0.73
February 2005	0.79	0.75
March 2005	0.78	0.74

On March 31, 2005, the Noon Buying Rate was USD 1.00 = EUR 0.77. These rates may differ from the actual rates used in the preparation of our financial statements and other financial information appearing in this annual report.

Capitalization and Indebtedness

Not applicable.

Reasons for the Offer and Use of Proceeds

Not applicable.

Risk Factors

You should carefully consider all the information in this annual report, including these material risk factors. The risks we face are not limited to the risks listed here. Some risks are not yet known to us and some of the risks that we currently do not believe to be material to our operations could prove to be material at a later date. All of these risks can materially affect our business, financial condition and results of operations.

We have a history of net losses and we expect to continue to incur net losses. We may not achieve or maintain profitability.

We have incurred net losses since our incorporation. At December 31, 2004, we had an accumulated deficit of €274,524. We expect to have net losses and negative cash flow in the foreseeable future. The size of these net losses and negative cash flow will depend, in part, on:

- the rate of growth, if any, in our licensing revenues;
- our ability to develop potential products either on our own or through partnerships, collaborations or strategic alliances; and
- the level of our expenses.

We may never generate sufficient revenues to achieve profitability. Our revenues are dependent on the success of our core technologies—in particular, PER.C6, AdVac and MAbstract phage antibody–display—and on our success and that of our licensees in developing commercially successful products based on these technologies. We do not have control over the ability of our licensees to develop commercially successful products based on our core technologies. We expect to continue to invest in order to enhance our core technologies and to invest in research and development of potential products. Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis.

We may need additional capital in the future. If we do not raise this additional capital, we may have to curtail or cease operations.

We expect that our future capital requirements will be substantial. Changes may occur that would consume available capital resources significantly sooner than we currently expect. If our capital resources are insufficient to meet future capital requirements, we will have to raise additional funds to continue the research and development of our technologies and potential products. We also may need to raise additional capital if we make any acquisitions involving cash consideration or the issuance of new shares. We may seek additional funding through public or private financing, strategic alliances or other arrangements. We may not have access to additional financing and, if we do, it may not be on favorable terms. If we fail to raise sufficient funds, we will have to curtail or cease operations, reduce our capital expenditures, scale back our development of new potential products, reduce our workforce and license potential products or technologies to others that we otherwise would seek to commercialize ourselves.

We expect that our interim results of operations will fluctuate, and this fluctuation could cause the price of our ordinary shares and American Depositary Shares (ADSs) to decline, causing investor losses.

Our interim operating results have fluctuated in the past and are likely to do so in the future. These fluctuations could cause the price of our ordinary shares and ADSs to fluctuate significantly or decline. Some of the factors that could cause our operating results to fluctuate include:

- the timing of entering into and the expiration of license agreements and collaboration arrangements;

- the success rate of our own and our licensees' discovery efforts leading to royalties and other payments;
- the timing and willingness of our licensees to commercialize products which would result in royalties and other payments; and
- general and industry specific economic conditions, which may affect our own and our licensees' research and development expenditures.

A large portion of our expenses is relatively fixed, including expenses for personnel, facilities and equipment. There is no direct link between the level of our expenses and our revenues. If revenues decline or do not grow as anticipated, we may not be able to correspondingly reduce our operating expenses and will suffer losses accordingly. In addition, we may increase our research costs in 2005, which may increase our operating expenses in the foreseeable future. Due to the possibility of fluctuations in our revenues and expenses, we believe that period-to-period comparisons of our operating results are not a good indication of our future performance. Our operating results in some periods may not meet the expectations of stock market analysts and investors. In that case, the price of our ordinary shares and ADSs would probably decline.

If we or our licensees do not develop potential products based on our core technologies that are approved for sale and are commercially successful, we may be forced to cease operations.

You must evaluate us in light of the uncertainties and complexities affecting our core technologies, none of which have yet been used to develop a product approved by the U.S. Food and Drug Administration for commercial use. Very little data exists regarding the safety and effectiveness of the type of potential products that we and our licensees are developing. All of our potential products, and those of our licensees, are either in research or in pre-clinical or clinical development. We and our licensees may not succeed in developing commercial products that are safe and effective, meet applicable regulatory standards, are capable of being manufactured at reasonable costs, or can be marketed successfully. We have not, and many of our licensees have not, yet begun to clinically test any of the potential products being developed using our core technologies.

Development of products requires significant investment, including pre-clinical and clinical testing, to demonstrate their effectiveness prior to their commercial distribution. We expect certain potential products to enter clinical trials during 2005. We and our licensees must conduct a substantial amount of additional research and development before any regulatory authority will approve any of our or their potential products. Our research and development or that of our licensees may not establish that our technologies or our or their potential products are safe and effective, in which case regulatory authorities may not approve them. Further, our government and university licensees and collaborators may have goals, such as academic publication or data collection, that are not solely focused on producing marketable products. We also rely heavily on research performed by third party collaborators that are not under our control in developing certain of our potential products. As a result, we are dependent on the research and performance of such third parties to bring potential products to market. Problems frequently encountered in connection with the development and use of new and unproven technologies and the competitive environment in which we and our licensees operate may further limit our and their ability to develop commercially successful products.

We rely on license and other revenues from the licensing of our PER.C6 and other technologies. If our licensees do not continue to use our PER.C6 technology or other of our technologies, or if they terminate their agreements with us, we will earn less or no revenue from our license agreements with them.

License revenues from our PER.C6 and other technologies have accounted for a substantial portion of our revenues to date and we expect that we will continue to be reliant on these revenues for the foreseeable future. If our current or prospective licensees do not develop and eventually distribute products based on our technologies, we may not be able to realize the revenues and growth we

anticipate. We also may not be able to successfully develop and derive license or other revenues from new technologies, such as the STAR technology that we acquired in 2004. Our current or prospective licensees may use or develop alternative technologies or develop competing products or potential products independently or in collaboration with others, including our competitors. The dollar/euro exchange rate may make our technology less competitive or reduce our revenues. If any of our licensees become involved in a business combination or other major corporate transaction, this could cause a strategic shift in their business focus and the technologies they use. Our agreements with our licensees do not require them to dedicate resources to developing and, eventually, distributing commercial products based on our technologies. Furthermore, our licensees may generally terminate their agreements with us on short notice. If they do terminate their agreements with us, we may not be able to enter into new arrangements to replace those agreements. During 2004, existing licenses with NatImmune A/S, Pfizer, Inc., Cell Genesys, Inc., Schering AG and Novavax, Inc., were not renewed. In the aggregate, annual payments from these license arrangements would have amounted to €536 in 2005.

We face competition in discovering, commercializing and licensing new technologies from biotechnology firms in Europe, the United States and elsewhere. This competition may limit our ability to derive revenues from our technologies and achieve profitability.

The field of biotechnology is new and rapidly evolving, and we expect that it will continue to undergo significant and rapid technological change. We operate in highly competitive markets and we may experience competition from companies that have similar or other technologies, or other products or forms of treatment for the diseases we are targeting. We are aware of a number of commercial initiatives in the fields in which we operate that may result in marketable products with which we would compete. We also may experience competition from companies that have acquired or may acquire technology from companies, universities and 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 or potential products that are more effective than those based on our technologies. We also compete with our licensees in developing new potential products. It is possible that we will not be able to effectively compete with these or other entities, and such competition could hamper our ability to bring products to market or license and derive revenue from our technology. Such an inability to compete could have a material adverse effect on our business, results of operations and ability to achieve profitability. For more information on our competitive position, see Item 4, "Information on the Company—Competition."

We are dependent on a small number of licensees for a majority of our revenues.

We are dependent on a small number of licensees that account for the majority of our revenues. For the year ended December 31, 2004, three licensees accounted for 56% of our revenues. For the years ended December 31, 2003, and December 31, 2002 three licensees accounted for 38% and 39% of our revenues, respectively. We currently are reliant on a limited number of contracts for revenues and commercialization of our PER.C6 technology, and any termination or alteration to these agreements would have a substantial adverse effect on our licensing revenues and financial results.

We are particularly reliant on our license agreements with sanofi pasteur and DSM Biologics ("DSM"). The licenses granted under these agreements are exclusive, which means we cannot license PER.C6 to other parties in connection with the development of the licensed influenza vaccine products or in the area of contract manufacturing for antibodies and therapeutic proteins. Such exclusivity may cause us to forego increased revenue opportunities from other third parties regarding the licensed technology over the terms of the agreements. Further, DSM is entitled to a portion of certain fees that are received with respect to its license, which could reduce the profitability of this technology to us. Finally, future payments to us under both agreements are dependent on reaching development

milestones, and we rely significantly on the performance and development progress of sanofi pasteur and DSM to reach the milestones set forth in each agreement. If these milestones are not reached, our revenues from these agreements could be substantially reduced. Though our license agreement with sanofi pasteur was initially with Aventis Pasteur (prior to the merger of Sanofi–Synthelabo and Aventis in 2004), we have no indication that the nature of our contractual relationship will be materially altered by the merger or otherwise.

We expect that a high level of licensee concentration will continue in the future. In the event that one or more of our major licensees were to terminate or substantially alter their licenses with us for any reason, we could experience a significant decrease in revenues and an adverse effect on our financial results.

In addition, while we have been successful in increasing our revenues from government grants and subsidies and private foundations, we cannot be assured that such grant and subsidy revenue will continue in the future.

Obtaining regulatory approval for our potential products and technologies is a costly and time-consuming process. If the relevant regulatory authorities do not approve products developed using our technologies, we or our licensees will not be able to commercialize them, and we may not receive any royalty or other revenues.

The U.S. Food and Drug Administration, or FDA, must approve any biopharmaceutical product before it can be marketed in the United States. Comparable authorities such as the European Medicines Agency, or the EMEA, the European Commission and local regulatory bodies regulate biopharmaceutical products elsewhere. In the approval process, a product candidate must undergo extensive testing, which can take many years and require substantial expenditures. The costs of pursuing and securing regulatory approval are increasing, necessitating additional regulatory compliance expenditure on our part. Required testing and trials include a review of the underlying technologies (including the cell line on which companies produce biopharmaceuticals) and are particularly rigorous with respect to vaccines. Product development involving new technologies is highly uncertain.

Although the FDA allows PER.C6 cells to be used to produce clinical materials for clinical trials at this time, the FDA has in the past raised concerns over the history and some of the properties of PER.C6 cells. New regulations could be adopted that would preclude use of PER.C6 cells in the future. If we or our licensees are unable to satisfy regulatory authorities as to the history and properties of PER.C6 or its appropriateness as a system which companies can use to produce biopharmaceuticals, PER.C6 could not be used to produce human biopharmaceuticals and our licensing and other revenues from PER.C6 will suffer. Our other technologies have not yet been used in clinical trials, and may face significant hurdles in obtaining regulatory approval if and when such trials begin.

If ethical, legal and social issues related to the use of genetic technology, human-based materials and animal testing negatively affect regulatory approval, patentability or market acceptance of our core technologies and of the products developed using these technologies, we would not be able to generate revenues from those products or our technologies.

The use of genetic technology and materials derived from human fetal tissue, such as PER.C6 technology, raises many ethical, legal and social issues that could hinder regulatory approval, patentability or market acceptance of our technologies and products developed using them. Further, public expressions of concern and adverse events involving new biopharmaceutical technologies or products (such as stem cells or genetically modified foods or organisms) could result in greater governmental regulation of our technologies and potential regulatory delays relating to the testing or approval of our own or our licensees' potential products. Advocacy groups have taken issue in the past and may take issue in the future with the use of genetic technology or materials derived from human fetal tissue, which may hinder or adversely affect regulatory approval or market acceptance of our

technologies and products developed using them. Concerns over the safety of new biopharmaceutical technologies or products could result in limited acceptance by patients and the medical community. In addition, we rely on animal testing in some of our research and development and adverse public reaction to our use of animal testing could also cause us to encounter negative publicity. Any of these factors could generate negative publicity or other adverse consequences regarding our business or industry, and could reduce or eliminate the potential markets for our own or our licensees' potential products.

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

Our commercial success depends in part on our ability to obtain and maintain adequate protection of our intellectual property rights in our technologies and potential products in Europe, the United States and elsewhere. If we do not adequately protect our intellectual property, competitors may be able to use our technologies and any potential products we develop and erode our competitive advantage and/or erode the value of our technologies.

Our commercial success also depends on not infringing patents and proprietary rights of third parties. Our work is in areas of technology where a large number of patent rights exist. As our activities in the biotechnology and biopharmaceutical markets expand and more patents are issued, the risk that our technologies and potential products may give rise to claims of alleged infringement increases. In addition, we may in the future wish to undertake activities, which raise patent infringement issues.

We routinely monitor the public disclosures of other companies operating in our industry regarding their technological development efforts to ensure that we do not undertake activities that infringe their intellectual property rights and to monitor whether those companies' activities may infringe our intellectual property rights. Due to the inherent imperfections of patent searching, we can never be certain that our monitoring will be exhaustive, and it is possible there may be third-party intellectual property rights of which we are not yet aware. If we determine that other companies' technological development efforts violate our intellectual property rights, we intend to take appropriate action. We are aware of a few patents which are potentially relevant to our past, current or anticipated activities. We believe that our current activities do not infringe any valid claims of these patents. Third parties, however, may seek to enforce patents against us and a court may find against us. Enforcing intellectual property rights against others or defending ourselves against claims of infringement can be very expensive, and any action in which we are involved could result in substantial costs and diversion of management and technical personnel and resources.

Other companies are and may become involved in proceedings regarding patents that cover technologies related to ours. The outcome of any intellectual property proceedings in which we or they are involved could effectively block our ability to further use or license our technologies or enter into co-development arrangements. It could also impair our or our licensees' ability to develop and commercialize potential products or products, and could result in the award of substantial damages against us. In the event of an unfavorable outcome in litigation, we may need to obtain licenses or redesign our technologies or potential products to avoid infringement. In the event that we must cease using a technology, we could encounter delays in license revenue generation, milestone or royalty payments or product introductions while we attempt to develop alternative technologies or potential products. If we do not succeed in such attempts, we may be forced to cease operations. In addition, if litigation results in a successful challenge to one of our patents, then competitors could be free to use the subject matter covered by the patent, or we may need to license the technology to others in settlement of such litigation.

In October, 2004 we commenced infringement litigation proceedings against CEVEC Pharmaceuticals in the District Court of Duesseldorf, Germany, arguing that CEVEC's cell line

infringes a recently granted European patent for our PER.C6 technology. In December 2004 CEVEC Pharmaceuticals acknowledged three out of four of our claims, but chose to defend the remaining claim. It is possible that the court will find against us on the remaining claim, and we cannot exclude the possibility that CEVEC will also file counterclaims in separate proceedings in order to attempt to have certain of our PER.C6 patents revoked or declared invalid.

If we or our licensees are unable to obtain any necessary licenses from third parties for use of their intellectual property on acceptable terms, we or our licensees may be unable to develop or market products based on our technologies.

We may be unable to earn revenues from products based on our technologies or from our own potential products if a third party does not grant us or our licensees a necessary license or offers a license only on unacceptable terms. Before we can market some of our potential products or technologies, we may need to obtain licenses from third parties who have patents or other intellectual property rights. For example, in the patent context, others have filed, and in the future are likely to file, patent applications covering technologies that we may wish to use or products that are similar to products that may be developed using our technologies. If these patent applications result in issued patents, we may need to obtain a license from the proprietors to use their patented technology. These licenses may not be available, or may not be available on acceptable or commercially reasonable terms. Without these licenses, we may be required to alter our technologies or potential products, or to avoid or stop certain activities. Our licensees may face similar problems.

If we lose the services of key personnel or are unable to attract and retain qualified personnel, we may be unable to develop our own technologies and potential products and to execute our business plan.

We are dependent on the principal members of our management and scientific personnel. We are particularly reliant on the members of our management board. Because of the experience our management board members have with our scientific research and development, our financial position and our business and the industry in which we operate, the loss of the services of any of them might adversely affect our results or the ongoing development of our technologies which is necessary to remain competitive and our ability to execute our business plan. The employment contracts of each of our management board members contain non-compete provisions that would apply for a period of one year after the end of their employment with us.

We also may not be able to recruit and retain the qualified personnel necessary to develop our core technologies and potential products and execute our business plan. There is currently a shortage of skilled executives, scientific personnel and intellectual property and regulatory experts in our industry, particularly in Europe. We believe this shortage is likely to continue. As a result, competition for skilled personnel is intense, and the turnover rate can be high. Competition for experienced executives, scientists, developers and manufacturers of pharmaceutical products, and other experts from numerous companies and academic and other research institutions may limit our ability to attract and retain qualified personnel on acceptable terms or may significantly increase our labor costs.

We may encounter difficulties in managing our growth. These difficulties could increase our losses.

We have experienced rapid and substantial growth and may continue to experience such growth in the future. This growth may be organic or through the acquisition of other companies or entities, and such growth will continue to place a strain on our human and capital resources. The aggregate number of full-time equivalent employees increased from 183 at December 31, 2002 to 210 at December 31, 2004. In addition, we will need to continue to expend funds to manage our operations and growth effectively. We will also need to continue to expend funds to attract and retain sufficient numbers of talented employees. If we do not have sufficient revenues to address these issues and otherwise make adequate expenditures, we may not be able to manage our growth effectively. If we are unable to manage our growth effectively, our losses could increase.

A number of our research and product development programs depend on access to biological materials without which we would be unable to conduct this research and development.

To continue to develop our core technologies and potential 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 appropriate biological materials, or if tighter restrictions are imposed on their use or on information generated from them, we could be restricted or prevented from conducting our research and product development. In addition, government regulations could result in restricted access to, or use of, human and other biological material samples.

We may have conflicts with our licensees that could make collecting payments due to us more difficult or that could negatively affect our relationship with our current and potential licensees.

We may have disagreements with our licensees over royalty payments due to us and may have difficulty in collecting these payments. Our existing license arrangements generally entitle us to receive royalty payments for any potential 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 their progress in these developments, we may not know of payments to which we would be 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 payments or, in some instances, we may not succeed in collecting these payments at all.

Our licensees may dispute the scope of the licenses that we have granted them, which could negatively affect our relationships with them and other licensees and our ability to grant additional licenses to other companies. A number of our license agreements provide that if more favorable royalty terms are granted to another licensee pursuant to a license of substantially the same scope, the initial licensee will also be entitled to the more favorable terms. A licensee may claim that other license agreements contain more favorable terms and that we should extend these terms to it. This may lead to a licensee disputing the amounts payable to us.

We rely on third-party suppliers for our serum-free medium and any interruption in this supply would interrupt our ability to conduct research and product development using PER.C6.

We and some of our licensees rely on third parties for the supply of the serum-free medium in which we grow our PER.C6 cells. Such media may not be available for sale on an industrial or bulk scale. We believe that alternative suppliers for a suitable serum-free medium could be found, but these alternative suppliers might not be able to meet our requirements rapidly or cost effectively. If supply problems forced us to use a new medium, we would need to spend time and resources to adapt our technology and processes to that medium, and, during this period of adaptation, our use of PER.C6 would be interrupted. Any such interruption or other failure of the serum-free medium upon which we currently rely could decrease the potential viability and profitability of our PER.C6 technology.

We have limited experience in conducting clinical trials and manufacturing, and no infrastructure for marketing or sales of pharmaceutical products. Our lack of experience and need to rely on third parties may delay our clinical trials or the marketing and sales of our potential products.

We have limited experience in conducting the clinical trials necessary to obtain regulatory approval. Consequently, we may encounter problems in clinical trials that would cause us or the appropriate regulatory authorities to delay, suspend or terminate these trials. These problems could include the inability to conduct clinical trials at preferred sites, enroll sufficient patients or begin or successfully complete clinical trials in a timely fashion, if at all. We also intend to use third parties to conduct clinical trials on our behalf and any failure of these third parties to perform under their arrangements with us in a timely manner may delay or terminate clinical trials. A delay or termination of clinical trials would result in a delay or inability to obtain the regulatory approval necessary for commercial distribution of potential products.

In addition, we do not have the experience or resources necessary to manufacture in large-scale quantities any products or potential products that we discover and develop, and we have no marketing or sales infrastructure. If we are not able to develop, or obtain through outsourcing arrangements, the requisite manufacturing, marketing and sales capabilities, we will be unable to commercialize our own products directly.

We may have significant product liability exposure, and our product liability insurance may be inadequate to cover product liability or other claims against us.

Like other organizations active in the biopharmaceutical industry, we may be exposed to product liability and other claims if third parties allege that our technologies, potential products or future products have caused harm. If a third party successfully sues us for an injury caused by our products, potential products or products developed using our technologies, our liability could exceed our total assets. Suits against us arising out of clinical trials may increase as more licensees utilize our technologies or potential products, thereby lessening our control over the manner of use of such technologies and potential products. Our general third party product liability insurance may not be adequate to address all of our product liability exposure. We may seek to obtain additional product liability insurance in the future, though such additional insurance may be prohibitively expensive, or may not cover all of our potential liabilities. If we are unable to obtain sufficient insurance coverage at an acceptable cost or if we are otherwise unable to protect ourselves against potential product liability claims, this could prevent or inhibit the commercialization of products that we or our licensees develop.

Third parties may bring claims relating to improper handling, storage or disposal of the hazardous materials we use in our business, which may require us to spend significant time and financial resources to defend and to pay damages.

Our research and development processes involve the controlled use of hazardous materials, including chemicals and radioactive and biological materials. Our BioSafety Level III (BSL-III) laboratory facilities allow us to work on-site with hazardous materials like West Nile virus that we were not permitted to work with before. Our operations also produce hazardous waste products. Given the inherently dangerous nature of certain of the materials we may work with in our BSL-III laboratory facilities and other hazardous materials incident to our work, we cannot eliminate the risk of accidental contamination or discharge and any resultant injury from these materials. Various applicable 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. In addition, claimants may sue us for injury or contamination that results from our use or the use by third parties of these materials, and our liability may exceed our total assets. Compliance with environmental laws and regulations may be expensive, and current or future environmental regulations may make us adopt more labor-intensive, time-consuming or complicated practices or procedures in connection with our research, development or production activities.

Conflicts of interest with our outside scientists may arise, which could limit our access to their expertise and impede the progress of our scientific research and development.

We work with scientific advisors and collaborators at academic and other institutions. These scientists are not our employees and may have other commitments that would limit their availability to us. If a conflict between their work for us and their work for another entity arises, we may lose their services. Because for some of our projects we rely to a significant extent on services of these outside scientists, if this were to happen, we may find it more difficult or expensive to continue such projects. Although our scientific advisors and collaborators generally sign agreements not to disclose our confidential information, it is possible that a certain portion of our valuable proprietary knowledge may become publicly known through them.

We cannot be certain that our licensing or other agreements are not in breach of applicable competition laws and will not be considered void.

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 our current or future similar agreements could be found to infringe applicable competition regulations. In this event, among other things, we may be subject to fines, claims of damages and our licensing or other agreements may be considered void and unenforceable. In 2004, a new regulation, the Technology Transfer Block Exemption Regulation, entered into force in the European Union, which may require us to review and possibly amend existing license and technology transfer agreements in the future to comply with the new regulation. This review process may be costly and time consuming and may require renegotiation of certain portions of our licenses and other agreements, but we do not expect this process to have a material adverse effect on our license portfolio or results.

The anti-takeover provisions in our articles of association and the laws of The Netherlands may prevent a change in control that may be in the best interests of our shareholders.

Our articles of association and the laws of The Netherlands may have anti-takeover effects. Among other things, our articles of association provide that the holders of our priority shares may make binding nominations for the election of our supervisory board members, and only a shareholders' resolution approved by an absolute majority of the votes cast, representing more than one-third of our outstanding shares, can set the nominations aside. One member of our management board, one member of our supervisory board and two independent members comprise the board of a foundation "Stichting Prioriteit Crucell", or the Priority Foundation, that holds all of our issued and outstanding priority shares. Furthermore, we may issue preference shares to another foundation under Dutch law, "Stichting Preferente Aandelen Crucell", or the Preferred Foundation, giving it preferred dividend rights and reducing the percentage of voting rights in the total number of votes to be cast by the holders of the other classes of shares. The chairman of our supervisory board, Pieter Strijkert, our chief executive officer, Ronald H.P. Brus 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 a change in control that might otherwise be in the best interest of our shareholders or offer them the opportunity to sell their ordinary shares or ADSs at a premium over the market price. See Item 10, "Additional Information" for additional information regarding the priority and preference shares and our articles of association.

Compliance with the internal controls and evaluations and attestation requirements under the Sarbanes-Oxley Act may be expensive and time-consuming.

Pursuant to Section 404 of the U.S. Sarbanes-Oxley Act of 2002, we will be required, as a foreign private issuer, beginning in fiscal year 2006, to perform an evaluation of our internal controls over financial reporting and have our auditor publicly attest to such evaluation. We have prepared an internal plan of action for compliance, which includes a timeline and scheduled activities, although as of the date of this filing we have not yet finalized the evaluation. Compliance with these requirements is expected to be expensive and time-consuming. If we fail to complete this evaluation in a timely manner, or if our independent auditor cannot attest to our evaluation in a timely manner, we could be subject to regulatory scrutiny and a loss of public confidence in our internal controls, with a corresponding adverse effect on our share price.

Our shareholders may have difficulty protecting their rights as a shareholder and in enforcing civil liabilities because 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 the liability of members of our management and supervisory boards. Our offices and all of our assets are located outside the United States. 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 United States. As a result, it may be difficult to serve process on us or these persons within the United States. It may also be difficult to enforce a U.S. court judgment against them in a U.S. court or in a Dutch court or to enforce a Dutch court's judgment against them in a U.S. court. This can include actions under the U.S. securities laws. In addition, it may be difficult to enforce, in original actions brought in courts in jurisdictions located outside the United States, liabilities under the U.S. securities laws. For a more complete discussion of potential difficulties in protecting your rights, see Item 10, "Additional Information—Enforcement of Civil Liabilities."

Our ordinary shares and ADSs may have a highly volatile trading price. You may not be able to resell your ordinary shares or ADSs at or above the price you pay for them, the ADSs may vary in value, and our share price may render us vulnerable to a takeover bid.

Our ordinary shares are listed on the Official Market of the stock market of Euronext N.V. (Amsterdam), also called the Amsterdam Stock Exchange. Our ADSs are quoted on the Nasdaq National Market. An active trading market for our ordinary shares or ADSs may not continue to develop or be sustained. The ADSs' low closing price during 2002, 2003 and 2004 has been \$2.50, \$3.81 and \$6.38 respectively, and the closing price as of March 31, 2005 was \$13.05. 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. Moreover, our share price and relatively high reserves of cash may indicate that we are vulnerable to an unsolicited takeover bid, as analysts have predicted a wave of mergers in the biotechnology industry involving companies that some investors may consider undervalued. In addition, any negative change in the public's perception of the prospects of biotechnology companies could depress our ordinary share or ADS price regardless of our results of operations. Other broad market and industry factors may affect the trading price of our ordinary shares and ADSs, regardless of our performance.

We believe that we were a passive foreign investment company in 2004 and expect to be classified as such in 2005, causing certain adverse U.S. tax rules to apply to investors.

We believe that we were a "passive foreign investment company" or "PFIC" for U.S. tax purposes in respect of the year 2004, and also expect to be classified as a PFIC in respect of the year 2005. Although we generally do not expect to be a PFIC in the long term, certain unfavorable U.S. tax rules apply to shareholders in companies that are PFICs in respect of even a single year. In order to minimize exposure to these rules, U.S. investors may wish to make a mark-to-market election. See Item 10, "Taxation—Taxation of U.S. Investors—Passive Foreign Investment Company Rules."

Item 4. Information on the Company

History and Development of the Company

We are a limited liability company incorporated in The Netherlands with the legal and commercial name, Crucell N.V. We were incorporated on October 9, 2000, as the holding company for Crucell Holland B.V., formerly called IntroGene B.V., following the merger of IntroGene B.V. and U-BiSys B.V. Our principal executive office is located at Archimedesweg 4, 2333 CN Leiden, The Netherlands and our telephone number is 31-71-524-8701. Our agent in the United States is CT Corporation, 111 Eighth Avenue, New York, New York 10011.

Business Overview

We are a biotechnology company developing vaccines and antibodies against infectious diseases. Our product programs comprise vaccines against influenza, West Nile virus, Ebola, malaria, and tuberculosis as well as an antibody product against rabies. Our programs are in various stages of pre-clinical development. We may choose to alter or expand our pipeline to include products that, in some instances, we may co-develop and market through collaborations or strategic alliances with third parties to share risks and costs. We also expect to continue licensing our core technologies to companies in our industry.

We generate revenues from the licensing of our proprietary technologies to pharmaceutical and biotechnology companies, from grants and government subsidies obtained to support the development of our vaccines and from service fees earned under development contracts with our partners. Neither our licensees nor we currently market any products based on our technologies. We intend to add 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. In addition, we expect our product development efforts to yield product revenues in the future. Our primary geographic markets are the United States and Europe.

The proprietary technologies which we use in making our own products, and license to other companies, may overcome the safety, efficacy, yield, and/or scalability limitations inherent in many currently available products, emerging products and manufacturing processes and technologies.

Our three core technologies are as follows:

- *PER.C6 technology.* Our PER.C6 technology encompasses a human cell line production system that our licensees and we use to develop biopharmaceutical products. The PER.C6 technology is currently being applied in four areas for the research, development and/or manufacture of:
 - (1) vaccines;
 - (2) antibodies and other therapeutic proteins;
 - (3) gene therapy products; and
 - (4) functional genomics, which is the study of how individual genes function.
- *AdVac technology.* Our AdVac technology is a recombinant vector technology that we use to develop novel adenoviral-based products. The AdVac technology is being developed to:
 - (1) improve upon existing vectors for vaccines and gene therapy;
 - (2) overcome the problems related to the presence of pre-existing immunity in target populations against the vector, which will potentially allow for more efficacious vaccines; and
 - (3) specifically target cells ex vivo that play an important role in enhancing a vaccine's efficacy.

- *MAbstract phage antibody–display technology.* Our phage antibody–display technology, which we use to display antibody fragments on the surface of a bacteria–infecting virus called a phage, can be used in the following ways:

- (1) to discover disease–associated molecules, which are molecules appearing on the surface of pathogens such as viruses, bacteria and parasites, or on diseased tissue, and which we refer to as drug targets; and
- (2) to develop human antibodies, which are antibodies that are derived from human DNA, as therapeutics against infectious disease, or in other disease areas.

Acquisition of ChromaGenics and STAR technology

In March 2004, we acquired the STAR technology through our purchase of ChromaGenics B.V., a privately held biotechnology company based in Amsterdam, for a purchase price of €4,017. In connection with the purchase, we also entered into a contingent payment agreement that could result in an additional payment of €7,000 upon our receipt of revenues generated from the STAR technology. STAR is a technology discovered by Dr. Arie Otte that may be useful for the production of proteins. It has a potentially broad application for production of proteins on mammalian cell lines such as our PER.C6 human cell technology and the widely used Chinese hamster ovary (CHO) cell line. STAR technology contains genetic elements that enable high–yield gene expression, thereby potentially reducing production costs. ChromaGenics was founded by UvA Holding B.V., Dr. Arie Otte, and Dr. Niek Roosdorp as a spin–off company of the University of Amsterdam. In a joint evaluation program funded by Genentech, we and Genentech are currently investigating whether STAR technology can increase the production yields of Genentech’s proprietary systems.

Strategy

Our mission is to be a leading biotechnology company developing products to combat infectious diseases. To achieve this mission, we pursue a business strategy aimed at developing and commercializing prophylactic vaccines and therapeutic antibodies to prevent and treat infectious diseases. We work together through strategic partnerships, collaborations, licensing agreements or other contractual agreements with leaders in the industry to increase broad acceptance and promote further usage of our technologies. Parallel to these efforts, we are developing our own portfolio of vaccines and antibodies. Some of these programs are partnered, like the development of new cell based influenza vaccines, while other programs are entirely developed in house, like the development of our West Nile virus vaccine. Apart from the main strategic focus on infectious diseases, we have allocated modest resources to build skills in protein and antibody production and to maintain our existing production technology as well as to develop the newly acquired STAR technology. The latter is currently undergoing joint evaluation by us and Genentech.

Our business strategy is based on the following business drivers:

- *Product pipeline offers competitive advantage.* We believe that each of our selected products either targets unmet medical needs in the area of infectious diseases, improves current medications, or is perceived as a marketable product due to predictive study models and/or due to perceived favorable regulatory conditions. We currently have five vaccine and one antibody programs in various stages of pre–clinical development, all of which are based on our PER.C6 production technology.

- *Our technologies provide unique points of difference to our products.* Our PER.C6 technology offers potentially significant competitive advantages in the development and commercialization of our products. The PER.C6 technology can be used to produce biopharmaceutical products that may demonstrate enhanced biological properties and prove to be potentially more

efficacious and less toxic than products derived from other production systems. The technology is also well suited for the production of certain human viruses that cannot be produced efficiently at present using alternative technologies. Our PER.C6 technology offers the ability to manufacture biopharmaceutical products in large volumes, which may speed the production process and reduce manufacturing costs. In addition, our AdVac vaccine technology has been shown to evoke a stronger immune response than other commonly used vaccine vectors, while our MAbstract technology has proved capable of fast identification of effective antibodies.

- *Ongoing technology licensing program.* In areas where we are not developing our own products, we offer our PER.C6 technology to the biopharmaceutical industry for the development and production of diverse biopharmaceutical products. This ongoing and extensive PER.C6 technology licensing program supports and accelerates our in-house product development by providing a source of revenue as well as the potential for future, additional revenue in the form of royalties from products developed by our licensees. We believe that our licensing program results in increased awareness in, and acceptance by, the biopharmaceutical industry of PER.C6 as a production technology for biopharmaceutical products. Our AdVac technology achieved its first exclusive license during 2004 and our new STAR technology is being evaluated by a potential licensee.

- *Our business model promotes progress on our programs while minimizing cash burn.* While we do not expect to reach profitability until our own products or products based on our technology reach the market, we believe our business model will support our financial position until those goals are met. Based on revenues derived from licensing, government grants and service fees, together with the selective external funding of our product programs, we expect this business model to enable us to execute aggressive product development programs while covering the resultant investment increases with these improving revenues and the funding of partners.

Our operating focus is on the progression of our product development programs to clinical trials, and we believe we have put in place the resources necessary to achieve this goal. We may decide to invest in new facilities and personnel in the future to maintain the proper infrastructure and resources needed to capitalize on available product development opportunities. We also may consider strategic acquisitions in the biotechnology industry and may enter partnerships to the extent such decisions may facilitate our strategy.

Industry/Scientific Overview

Manufacturing Systems for Biopharmaceutical Products

Biopharmaceutical products are therapeutics produced by means of biological production systems. Modified bacteria and yeast initially were used to produce the first generation of human biopharmaceutical products. The first available human cell-based production systems employed human cells that spontaneously acquired the ability to divide indefinitely. These include the MRC-5 and WI-38 cell lines, which were both derived from human lung tissue. These cell lines have been successfully used to produce a number of human vaccines (rubella, mumps, measles, rabies and hepatitis A). More recent and better defined human cell lines were created by extracting a small and well defined part of the genome (E1) from the adenovirus type 5 and inserting this into healthy primary human cells where it subsequently causes stable, indefinite cell growth. The immortalized cell and its progeny are called a "cell line." A number of examples of cell lines that were made by E1 immortalization, like 293 and 911, have been described in literature and were made for research purposes. To our knowledge, the only documented cell lines based on E1 immortalization principle that were made specifically for production of biopharmaceuticals, are PER.C6 and N52.E6.

Vaccines

Vaccines are designed to protect people against potentially life-threatening diseases, including those caused by parasites, viruses and bacteria.

Scientific Progress in Vaccines. Vaccines have contributed significantly to the improvement of global public health in the twentieth century. Smallpox was eradicated through the use of vaccines, and polio is well on its way to eradication. 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 viruses such as HIV, influenza, Ebola and West Nile virus; against parasites causing malaria; and also against inherited or acquired diseases such as cancer.

Vaccine Formats. A variety of vaccine formats are in use today and others are evolving through ongoing research and development efforts. Some of the most common vaccine formats include live-attenuated virus vaccines, inactivated whole-killed virus vaccines, subunit 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 overall vaccine efficacy. The key objectives of current vaccine technology research and development are to make safer vaccines without compromising efficacy, to generate new vaccines with stronger and broader immunogenicity, to make vaccines using more efficient manufacturing processes and to make vaccines easier to administer.

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 or bacteria. Antibodies recognize and bind to invading pathogens, ultimately eliminating them. Thus, antibodies play 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 trigger the death of a target cell or bind to and block a key interaction of a disease-related cell, such as a cancer cell; to develop therapeutic products that block infectious agents; bind and neutralize toxic products; as tools in scientific research such as genomics and proteomics; and to develop diagnostic products to detect viruses or bacteria.

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 is the technology whereby human antibody genes are 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.

CruCell Core Technologies: PER.C6 technology

Overview

Our PER.C6 technology provides a manufacturing system that consists of a human cell line, which can be used to produce a variety of biopharmaceutical products. We developed the PER.C6 technology from a single source of healthy, human retina cells in a controlled, documented manner. To obtain our PER.C6 cell line, we have inserted an exactly defined fragment of the E1 region of the genome of the adenovirus type 5 into a healthy human retina cell so that the cell can grow indefinitely. The PER.C6 cell line has been successfully adapted to grow without the need for serum components or materials that allow cell attachment (microcarriers) and demonstrates excellent cell densities in bioreactors. These features of our cell line are important to produce safe biopharmaceutical products in sufficient quantities.

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

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

For classical vaccine production, PER.C6 cells are infected with the virus against which the vaccine is meant to protect. The virus is subsequently multiplied on PER.C6 cells to high virus titer, yielding a potent starting material that can be processed and purified to produce a final formulation of a whole-killed, split or subunit vaccine.

For recombinant vaccine production, the PER.C6 technology produces delivery agents called adenoviral vectors. These vectors have been made replication incompetent and thus are only capable of delivering into the human body a portion of DNA encoding for a protein from the pathogen against which the vaccine is meant to protect. The DNA inserted into the vector can be derived from a virus, a parasite or even bacteria, providing a versatile vaccine vector platform.

Protein production. PER.C6 technology can be used as a production system for developing and manufacturing both antibodies and other proteins. For both antibody and protein production 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 protein.

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 human virus—that carries therapeutic genes and facilitates the delivery of the gene into the cells. Since the PER.C6 cell line 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 can be inserted to perform studies of gene functions. The adenovirus libraries carry many genes with unknown functions, which can be used to determine the function of individual genes in a disease process. We believe that PER.C6 technology, therefore, represents a key analytical tool in the discovery of new genes and their role in biological pathways and human disease. Galapagos Genomics, a functional genomics company in which we hold a 20.8% ownership share, executes these activities exclusively using our PER.C6 technology. Please refer to the "Galapagos Genomics" section of Item 4 for additional information about this joint venture.

Key Features and Advantages

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

- **High Yields.** PER.C6 technology potentially offers a system for high yield, large-scale biopharmaceutical product production. PER.C6 can be cultured at high densities and engineered to produce large quantities of biopharmaceuticals, which helps reduce production expense.
- **Scalability in Serum-free Conditions.** PER.C6 cells can be cultured in a serum-free medium, without micro-carriers, in a closed bioreactor vessel. This simplifies the expansion from laboratory- to industrial-scale production, potentially leading 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 our PER.C6 technology, which may facilitate regulatory approval.
- **Biologics Master File at the FDA.** We have filed a Cell Substrate Biologics Master File (BMF) with the U.S. Food and Drug Administration (FDA) describing our PER.C6 technology, including its establishment, development and potential use in production processes. The FDA will only evaluate the PER.C6 technology in the context of (investigational) new drug applications. We believe that the information in our BMF will facilitate the FDA's appraisal of any biopharmaceutical product that our licensees or we produce using the PER.C6 technology.
- **Broad Industry Endorsement.** PER.C6 can now claim to have achieved a broad endorsement within the industry, with more than 35 licensees. A number of products are in clinical development, including an HIV vaccine at Merck and a monoclonal antibody with AME/Eli Lilly.
- **Human-based.** We believe that antibody and other protein products based on the human-based PER.C6 technology will 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.

CruCell Core Technologies: AdVac technology

Overview

We use our AdVac technology, in combination with our PER.C6 production technology, to develop recombinant vaccines.

While no adenovirus-based recombinant vaccines are currently licensed for human use, the scientific community is testing the ability of these vaccines to counter viruses (HIV, hepatitis C and Ebola), parasites (malaria) and bacteria (anthrax), to name a few. Recombinant vaccines are necessary for these diseases since inactivated whole virus vaccine approaches are either ineffective against these particular pathogens, or are too difficult or dangerous to produce. Within the field of vaccination and gene therapy, adenovirus serotype 5 (Ad5) is the most commonly used vector.

The portion of the human population that has been exposed to Ad5 is high, and early clinical trial data demonstrates a clear correlation between the level of pre-existing immunity against Ad5 and the frequency of non-response against Ad5-based vaccines. Moreover, immunity and resistance to Ad5 has been proven to vary from person-to-person, creating difficulties with respect to vaccine dosing issues.

We designed the AdVac technology to manage the problem of pre-existing immunity in humans against the recombinant adenovirus serotype 5 (rAd5) vaccine vector, without compromising large-scale production capabilities or the immunogenic properties of rAd5. AdVac technology is based on adenovirus vectors that do not regularly occur in the human population, such as Ad35 and Ad11. The

technology supports the practice of inserting DNA coding for pathogen—derived proteins into a vector. AdVac technology may also be used to develop *ex vivo* vaccines and gene therapy products.

Key Features and Advantages

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

- ***Safety and Efficacy.*** Because AdVac technology is based on adenovirus vectors not commonly found in the human population, pre-existing immunity to the vector is rare. This may allow for lower dosage schedules.
- ***Scale and Manufacturing.*** The cell cultures that complement AdVac technology are based on PER.C6 technology, and we expect AdVac technology to help make large-scale manufacturing of recombinant vaccines possible. We believe that the biopharmaceutical industry requires this capability to meet the global demand for vaccines required to eradicate existing and emerging infectious diseases.

Crucell Core Technologies: MAbstract technology

Overview

Our MAbstract technology can be applied for the discovery of novel drug targets and the identification of human antibodies against those drug targets. The 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 contacted with pathogens, or cells suspected of carrying the drug target, or if the target is already known in advance, the library may be contacted 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 subtract irrelevant phage-antibodies present in the library. Since irrelevant phage-antibodies for the target in question are often present in great abundance, the subtraction 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 function in binding 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, or 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 using transgenic mice. These advantages include the following:

- ***Subtraction Method of Selection.*** MAbstract technology selects antibodies for possible therapeutic use and discovers novel drug targets using whole cells, tissues or infectious agents. The

subtraction method of selection is not available when generating human antibodies in transgenic mice.

No Inherent Limitation on Antibody Specificity. MAbstract technology does not have the inherent limitation on antibody specificity that is seen in transgenic mice.

Production Using PER.C6 technology. 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.

Licensing and Collaborations

Licensees and partners. Our current licensees and partners are as follows:

VACCINES

PARTNER/LICENSEE	STARTING DATE	TECHNOLOGY	DISEASE TARGET	DEVELOPMENT STAGE
Aeras Global TB Vaccine Foundation	Mar. 2004	PER.C6 and AdVac	Tuberculosis	Pre-clinical
sanofi pasteur	Dec. 2003	PER.C6	Influenza	Pre-clinical
Chiron Corp.	Dec. 2004	PER.C6	Alphavirus vectors	Pre-clinical
Harvard School of Medicine	Oct. 2002	PER.C6 and AdVac	SIV	Pre-clinical
International AIDS Vaccine Initiative (IAVI)	Sep. 2004	AdVac	HIV	Pre-clinical
Kimron Veterinary Institute	Jul. 2003	PER.C6	West Nile virus—Veterinary vaccine (avian)	Market authorization in Israel
MedImmune Inc.	May 2002	PER.C6	Influenza-related	Pre-clinical
Merck & Co. Inc.	Oct. 2000	PER.C6	Hepatitis C	Pre-clinical
Merck & Co. Inc.	Oct. 2000	PER.C6	HIV	Phase II
Merial LLC	Oct. 2004	PER.C6	Foot and mouth disease	Pre-clinical
National Institutes of Health (NIH)	Mar. 2002	PER.C6 and AdVac	Ebola, Lassa and Marburg	Pre-clinical
National Institutes of Health (NIH)	Mar. 2004	PER.C6 and AdVac	Malaria	Pre-clinical
New York University	Aug. 2002	PER.C6 and AdVac	Malaria	Pre-clinical
Vaxin, Inc.	Sep. 2004	PER.C6	Respiratory viruses	Pre-clinical
Walter Reed Army Institute of Research & GlaxoSmithKline	Mar. 2003	PER.C6 and AdVac	Malaria	Pre-clinical
Biologicals	Mar. 2003	PER.C6 and AdVac	Malaria	Pre-clinical
Singvax	Mar. 2005	PER.C6	Japanese Encephalitis	Pre-clinical

ANTIBODIES AND THERAPEUTIC PROTEINS

PARTNER/LICENSEE	STARTING DATE	TECHNOLOGY	DISEASE TARGET	DEVELOPMENT STAGE
Applied Molecular Evolution, Inc. (Lilly)	Oct. 2002	PER.C6	Portfolio antibodies	Phase I
Biogen Idec, Inc.	Dec. 2003	PER.C6	Undisclosed	Pre-clinical
Centocor Inc. (Johnson & Johnson)	Dec. 2002	PER.C6	Portfolio antibodies	Pre-clinical
Chiron Corp.	Jun. 2004	PER.C6	Portfolio antibodies	Pre-clinical
GlaxoSmithKline Ltd	Aug. 2004	PER.C6	Portfolio antibodies	Pre-clinical
Innogenetics	Jan. 2002	PER.C6	Portfolio antibodies	Pre-clinical
JCR Pharmaceuticals Co. Ltd	Mar. 2005	PER.C6	Undisclosed proteins	Pre-clinical
Merck & Co., Inc.	May 2003	PER.C6	Portfolio antibodies	Pre-clinical
Merus B.V.	Jun. 2004	PER.C6	Portfolio oligoclonics	Pre-clinical
Micromet AG	Nov. 2004	PER.C6	Portfolio antibodies	Pre-clinical
Millipore Corp.	Mar. 2003	PER.C6	Undisclosed	Pre-clinical
MorphoSys AG	Sep. 2004	PER.C6	Portfolio antibodies	Pre-clinical
PanGenetics	Jun. 2004	PER.C6	Portfolio antibodies	Pre-clinical
Roche	Jan. 2005	PER.C6	Undisclosed proteins	Pre-clinical
Synergistics/Synco Biopartners Investments B.V.	Aug. 2004	PER.C6	Portfolio antibodies	Pre-clinical
Genentech	Feb. 2004	STAR	—	Evaluation
Mitsubishi Pharma Corporation	Mar. 2005	PER.C6	Undisclosed proteins	Pre-clinical

GENE THERAPY

PARTNER/LICENSEE	STARTING DATE	TECHNOLOGY	DISEASE TARGET	DEVELOPMENT STAGE
Edwards Life Sciences Corp.	Nov. 2004	PER.C6	Portfolio	Pre-clinical
EMD Lexigen Pharmaceuticals Corp. (Merck KgaA)	Dec. 2001	PER.C6	Portfolio	Pre-clinical
Eurogene Ltd (Ark Therapeutics)	Nov. 2000	PER.C6	Portfolio	Pre-clinical
GeneMax Pharmaceuticals Inc.	Aug. 2003	PER.C6	Portfolio	Pre-clinical
GenVec Inc.	Jul. 2002	PER.C6	Cardiovascular	Phase II
GlaxoSmithKline Ltd.	Feb. 1999	PER.C6	Portfolio	Pre-clinical
Merck & Co., Inc.	Nov. 1998	PER.C6	Portfolio	Pre-clinical
ML Laboratories Ltd.	Jun. 1998	PER.C6	Portfolio	Phase I/II
NeoTropix	Mar. 2004	PER.C6	Oncology	Pre-clinical
Selective Genetics Inc.	Jun. 2001	PER.C6	Portfolio	Phase I/II
Transgene SA	Apr. 2001	PER.C6	Portfolio	Phase I/II
Wyeth	Jul. 2004	PER.C6	Non-disclosed	Pre-clinical
Vascular Biogenics Ltd	Mar. 2005	PER.C6	Portfolio	Pre-clinical

ALLIANCES WITH CONTRACT MANUFACTURERS FOR PRODUCTION

PARTNER/LICENSEE	STARTING DATE	TECHNOLOGY	AREA
Cambrex	Aug. 2004	PER.C6	Medium development
DSM Biologics	Dec. 2002	PER.C6	Therapeutic proteins (including antibodies)
Gene Medicine Japan, Inc.	Oct. 2003	PER.C6	Recombinant vaccines & gene therapy products (Asia)
Hyclone, Inc.	Dec. 2003	PER.C6	Medium development
Invitrogen Corp.	Jun. 2003	PER.C6	Medium development
JRH Biosciences Inc.	May 2004	PER.C6	Medium development
Molecular Medicine BioServices, Inc.	Dec. 2001	PER.C6	Recombinant vaccines & gene therapy products (USA)
Sigma–Aldrich Corp.	Dec. 2003	PER.C6	Medium development

FUNCTIONAL GENOMICS

PARTNER/LICENSEE	STARTING DATE	TECHNOLOGY	AREA
Galapagos Genomics N.V.	Jun. 1999	PER.C6	Genomics

License agreement structure. Our customers can elect to take either a license for commercial development or a license for research only. In addition, we have issued exclusive licenses to certain licensees. Our research licenses granted in the areas of antibodies and gene therapy typically cover the entire portfolio of antibodies and genes, respectively, that the customer may wish to use in the future. The general payment structure under the terms of our commercial licenses is as follows:

- **One–time issuance fee.** We charge our licensees a one–time issuance fee, the amount of which is determined by the nature of the licenses, e.g., whether the license is for commercial development or research use, whether the license is exclusive or non–exclusive, and the area of use of the license.
- **License maintenance.** Our licensees pay annual fixed payments to maintain their licenses. The license maintenance fee is paid annually and generally offset against any royalty payments accruing from the time of initial commercial sales.
- **Milestone payments.** Certain licenses provide for additional fees to be paid if the applicable licensee achieves certain agreed upon targets, or milestones. Milestone payments are typically not offset against future royalty payments.
- **Royalty payments.** With the exception of a limited number of licenses (including Transgene SA, MedImmune, Millipore and Galapagos Genomics), we will receive a percentage of the value of any net sales that the licensee may generate related to the eventual product. Royalty payments are typically only payable once they exceed the license maintenance fees. Our license agreements generally do not contain stacking provisions, meaning that royalty payments are not reduced in the event that total payments by the licensee to all licensors go above a certain percentage. We have received minor royalty payments from one licensee, Molecular Medicine BioServices, Inc., a contract manufacturing organization that licensed our PER.C6 technology to offer manufacturing recombinant vaccines and gene therapy products.
- **Service fees.** As part of various collaboration agreements, we receive service fees for work performed under such agreements.

Research licenses provide for lower issuance and license maintenance fees and do not provide for royalty payments. Generally our research licenses provide that the license may be converted into a commercial license, and furthermore typically do not allow (late) clinical development and commercial distribution of any product using the licensed technology.

Our commercial license agreements generally provide that the applicable commercial license will expire after the expiration of the last applicable patent or 10 to 15 years after the first commercial sale of a product developed under the agreement with that licensee. Our research licenses generally expire two to five years after their effective date. Most of our licenses may be terminated on 90 days' notice from the licensee. Generally, licensees may assign or sub-license their rights. Under our license agreements, because the technology that we transfer is fully-developed, we are not required to deliver any updated technology to any of our licensees, though we update our know-how with respect to our technology from time-to-time through Biologics Master Files to which our licensees have access.

Exclusive Licenses. We have issued certain licenses to licensees 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. For example, our agreement entered in December 2003 with Aventis Pasteur (now sanofi pasteur) for the development and commercialization of PER.C6-based influenza vaccines includes provision for milestone payments, annual payments and research and development funding, as well as high single-up to double-digit royalties on future PER.C6-based influenza vaccine sales. The agreement also includes financial diligence provisions designed to encourage sanofi pasteur to obtain successful regulatory approval in the United States (FDA registration and approval) and Europe (EMEA registration and approval) for the PER.C6-based influenza vaccine as promptly as possible. In 2004, we granted an exclusive license to the International AIDS Vaccine Initiative (IAVI) for the development of an AIDS vaccine based on our AdVac technology. Other exclusive licenses include our agreements with DSM Biologics for the contract manufacturing of recombinant proteins and monoclonal antibodies under PER.C6 licenses and Merck & Co. for a PER.C6-produced HIV/AIDS vaccine. An extension to our agreement with Merck relates to our PER.C6 Cell Substrate Biologics Master File (BMF), BB-MF 8453 in the U.S., and equivalents in other jurisdictions. We will work with Merck on matters relevant to maintaining the BMF, including the provision of technical assistance and guidance from Merck as appropriate. We believe that this agreement broadens our relationship with Merck and helps to ensure that our BMF will be upgraded in line with evolving regulatory guidelines.

Manufacturing Services

We follow good manufacturing practice level (GMP) manufacturing services for our customers. We have built a small-scale production facility in Leiden, The Netherlands, and in 2000 we obtained the license required for the manufacture of clinical trial materials at this facility from the Dutch regulatory authorities. To date we have used the facility to manufacture clinical grade adenoviral vectors. The production facility consists of classified clean rooms suitable for manufacturing of purified bulk drug product. We continuously explore additional or alternative uses for our GMP production facility. Production and testing is done under quality assurance control. Full batch documentation is generated and reviewed for product release according to EU and U.S. regulations.

We have signed manufacturing service agreements with a few of our customers. Under these agreements, we have produced and may produce in the future clinical batches of adenoviral materials or other materials using our PER.C6 cell line 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 specifications of the agreement.

Research and Development

Overview

Our PER.C6 technology, complemented by our AdVac and MAbstract technologies, drives the development of our current 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 currently have several potential products in various stages of pre-clinical development. We may enter into collaborative and/or strategic alliance arrangements with third parties to co-develop and market products that we may develop.

Our primary focus is the development of a range of novel vaccine and antibody products in the area of infectious diseases. We currently have five core programs in various stages of pre-clinical development, together with two early-stage discovery programs:

PER.C6. Our core influenza (as part of our collaboration with sanofi pasteur) and West Nile virus vaccines are both being produced using our PER.C6 technology.

PER.C6 and AdVac. Our Ebola and malaria vaccines are recombinant vaccines based on PER.C6 that also use AdVac technologies. In addition to these core programs, a new collaboration with the Aeras Global TB Vaccine Foundation was announced in March 2004 for the pre-clinical and clinical development of candidate tuberculosis (TB) vaccines based on PER.C6 and AdVac.

PER.C6 and MAbstract. In 2003 our Antibody Discovery Group also turned its attention towards infectious diseases, and in 2004 the discovery of its first two human monoclonal antibody products was announced. The first, for protection against SARS, is currently on hold, while our rabies antibodies announced in November 2004 becomes an additional core product program.

A short description of each of our potential products, and the diseases those products target, follows.

Influenza

Each year approximately 10–20% of the world's population contracts influenza, and an estimated 250,000 to 500,000 people die annually from influenza-associated complications. 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.

Influenza vaccines are classically produced on embryonated chicken eggs. However, various challenges have led the biopharmaceutical industry and the scientific community to explore other ways of producing influenza vaccines. Currently, cell culture systems are being developed for influenza vaccine production based on African Green Monkey Kidney (VERO) cells and Madin Darby Canine Kidney (MDCK) cells. These cell systems often need to be grown on micro-carriers, which makes the production process expensive and difficult to scale. In contrast, PER.C6 cells grow well in suspension and are easily scalable, potentially permitting the production of cost-efficient vaccines in large quantities. Virus yields on VERO cells have been shown to be significantly lower than the yields grown on PER.C6 cells. PER.C6 can produce all influenza strains that we have tested, possessing the different receptors required for the production of both human strains and the avian strains that may present a pandemic threat.

Based on these factors, we made the decision in the second half of 2003 to go forward with our influenza vaccine product development based on an inactivated split virus vaccine concept. In this

regard, influenza vaccines are well defined as a product. The safety and efficacy of such influenza virus vaccines is proven—vaccine production is the main challenge.

In December 2003, we entered into a strategic agreement with sanofi pasteur to further develop and commercialize novel influenza vaccines using our PER.C6 production technology. Please refer to the "Licensing—Exclusive Licensees" section of Item 4 for more information about this agreement. Sanofi pasteur is the world leader in vaccines, and has been the largest supplier of influenza vaccines for more than 50 years, providing more than 100 million doses worldwide during the 2003–04 season. Since the inception of the collaboration, production processes have been under development, with the production of a GMP master cell bank already completed. Sanofi pasteur has contracted a leading CMO for an engineering concept study for vaccine production in 20,000 liter bioreactors. We expect the collaboration to commence clinical trials in 2005.

West Nile Virus

Named for the West Nile district of Uganda where the disease was discovered in 1937, West Nile virus infection can lead to mortality in humans and animals by causing a fatal form of encephalitis, or inflammation of the brain. It is estimated that 20% of the people who become infected with West Nile virus will develop West Nile fever. Persons over 50 years of age have the highest risk of developing a severe disease, such as meningitis, an inflammation of the membrane around the brain and the spinal cord, or encephalitis. Since 1999, West Nile virus has caused disease in more than 16,000 U.S. citizens, leading to 650 deaths.

Continued efforts are being made to find suitable treatments and vaccines to stop this virus. The virus may become a recurring threat in the United States. In 2003 and 2004, a number of West Nile virus cases were reported in Europe.

In June 2003, we announced our decision to develop a vaccine against the West Nile virus based on our PER.C6 technology. Our vaccine uses an inactivated whole virus concept, which is different from vaccines currently under development by our competitors. Currently there is no vaccine or antiviral therapy available to protect humans against West Nile virus.

In a separate but related program, we entered collaboration with Kimron Veterinary Institute of Israel in June 2003, granting Kimron a license to our PER.C6 technology to develop a West Nile veterinary vaccine for use in geese and other birds susceptible to the virus in Israel. This veterinary vaccine achieved market authorization in Israel on June 3, 2004 and we expect that it will be produced for distribution prior to the 2005 West Nile season. Kimron intends to replace its existing West Nile veterinary vaccine, which is produced using mouse brain cells, with the PER.C6–based vaccine. Under the terms of the agreement, Kimron has commercial rights to the PER.C6–based West Nile veterinary vaccine in Israel.

The significance to our human vaccine program is that a PER.C6–based vaccine protects against the Israel 1998 Goose strain of West Nile virus. The fact that this strain is closely related to the New York 1999 strain, which caused the West Nile outbreaks in the U.S., supported our decision to develop a West Nile vaccine for humans. We intend to enter clinical trials with our human West Nile virus vaccine in the fourth quarter of 2005. An agreement with the Netherlands Vaccine Institute (NVI) was announced in November 2004 for the manufacture of the vaccine at NVI's new BSL–3 (BioSafety Level 3) plant for use in the human clinical trials.

Ebola

Ebola fever is one of the most lethal viral diseases, with a mortality ranging from 50% to 80%. Ebola outbreaks occur regularly in tropical Africa, affecting both human and great ape populations. To date, approximately 2,000 cases have been reported since the virus was first discovered in 1976. The

Ebola virus belongs to the group of "hemorrhagic fever viruses," which also includes the highly pathogenic Marburg and Lassa viruses. Ebola virus causes a disease characterized by high fever and massive internal bleeding. Because no vaccine or therapy is presently available, Ebola virus is on the Centers for Disease Control (CDC), National Institutes of Allergy and Infectious Diseases (NIAID), and U.S. Department of Defense Category "A" list of bioterror agents. In 2003 the U.S. government announced that once available, an Ebola vaccine will be stockpiled as part of its preparedness for bio-terror attacks under Project BioShield, a comprehensive effort to develop and make available modern, effective drugs and vaccines to protect against attack by biological and chemical weapons. The BioShield Act was passed by Congress and signed by President Bush in July of 2004, with a total appropriation of US\$5.6 billion across all programs.

Numerous attempts to vaccinate against Ebola virus using inactivated virus or protein-based vaccine modalities have failed, and developing a live attenuated vaccine is considered too dangerous. However, it has been shown that a single-dose immunization with a recombinant adenovirus (expressing Ebola virus proteins) vaccine protects monkeys against an otherwise lethal challenge with wild-type Ebola virus. Based on these results, we decided to develop an Ebola vaccine. The vaccine could provide protection from the lethal virus in the event of biological warfare.

We have entered into a Collaborative Research and Development Agreement (CRADA) with the Vaccine Research Center (VRC) of the National Institutes of Health (NIH) in the United States 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. The recombinant vaccine will encompass the glycoproteins and the nucleoprotein of Ebola virus, but cannot replicate in humans. This method thus provides a very important safety advantage, while ensuring that a strong humoral and cellular immune response is elicited against the Ebola virus. Under a separate production contract with NIH, we are manufacturing adenovirus Ebola vaccine vectors according to current good manufacturing practice (cGMP) requirements. In March 2005 we extended the CRADA with NIH and continue to develop this vaccine and will use the Ebola vaccine results in the development of Marburg and Lassa vaccines. In addition, we obtained an exclusive license to certain NIH patents to develop and commercialize recombinant vaccines against Ebola. The patents cover valuable vaccine components, such as Ebola antigens and vectors. In addition, the license covers 'one-shot' emergency vaccination strategies that have proven to be effective in relevant animal models.

In experiments conducted by the VRC together with the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) during the first half of 2004, our vaccine candidate confirmed single-dose protection of monkeys 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. All preclinical material was produced at Crucell's FDA-compliant production facilities in Leiden. The positive results have seen clinical trial initiation set for the fourth quarter of 2005.

In 2002 the FDA issued the so-called "two animal" or animal efficacy rule, which states that efficacy studies in man are not required to obtain a product license for special categories of products as long as efficacy is established in two independent animal models and safety in man. Our Ebola vaccine may be a candidate for regulatory approval under this rule, and the use of the two animal rule could potentially speed up the approval process for our Ebola vaccine.

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 one of today's top three killers among communicable diseases. The disease currently represents one of the most prevalent

infections in tropical and subtropical areas causing severe illness in 300 to 500 million individuals worldwide, and causing one to three 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 10–30%. The widespread occurrence and elevated incidence of malaria are a consequence of discontinued malaria control programs and increasing numbers of drug-resistant parasites and insecticide-resistant parasite vectors. Other factors include environmental and climatic changes, civil disturbances and increased mobility of populations. Although the overwhelming majority of morbidity and mortality associated with malaria occur in the developing world, this disease also affects travelers.

Currently there is no commercially available vaccine to protect against malaria. Our candidate malaria vaccine is based on our AdVac technology and produced using our PER.C6 technology. In a study carried out by the Department of Medical Molecular Parasitology at New York University, the efficacy of our malaria vaccine candidate was tested in NYU's mouse malaria model. The study showed that a single administration of a prototype AdVac vaccine, a recombinant adenovirus 35 (rAd35) vector expressing the malaria parasite-derived immunogenic circumsporozoite antigen, protects mice upon challenge with the mouse specific parasite.

In March 2003, we entered into collaboration with the Walter Reed Army Institute of Research (WRAIR) and GlaxoSmithKline Biologicals (GSK) under a Cooperative Research and Development Agreement (CRADA). Pursuant to this agreement, we have been working with WRAIR and GSK to evaluate our AdVac malaria vaccine candidate directed against the human malaria parasite *Plasmodium falciparum*. Our vaccine candidate is being tested as a stand-alone vaccine and in combination with GSK's RTS,S malaria vaccine candidate. The GSK malaria vaccine candidate RTS,S has been shown to confer partial protection to human volunteers in both a laboratory challenge model conducted at WRAIR and under natural challenge conditions in a field study conducted in the Gambia. Phase IIb pediatric trials conducted in Mozambique and reported in *The Lancet* medical journal in October 2004 demonstrated further promising results, with the vaccine protecting some infants against infection and making the course of the disease less serious and life threatening in others.

Studies in monkeys conducted during 2004 as part of the CRADA resulted in excellent immune responses for our AdVac-based malaria vaccine. Further, in March 2004 it was announced that the National Institute of Allergy and Infectious Diseases (NIAID), part of the U.S. National Institutes of Health (NIH), will support the development of our candidate malaria vaccine. The agreement has an estimated value of up to US\$3.5 million and will cover process development of the candidate AdVac-based malaria vaccine including the production of clinical trial material and Investigational New Drug (IND) filing. The work will be done under a subcontract agreement with Science Applications International Corporation (SAIC). It is expected the vaccine will enter the clinic in the second quarter of 2006.

A further boost to the program was received at the end of 2004 with the December announcement of a grant up to a maximum of EUR 2 million from the Dutch Ministry of Economic Affairs in support of our malaria research and AdVac technology development. Research carried out under this grant will aim to expand the number of antigens able to be carried by an rAd35-vectored vaccine, such as our AdVac-based malaria candidate.

Tuberculosis

Mycobacterium tuberculosis (TB) represents one of the most prevalent infectious diseases throughout the world. It is estimated that 2 billion people are infected with TB, representing a third of the world's population. Each year sees 8 million new cases and 2 million deaths as a result of the disease.

TB is spread when people who have the active form of the disease cough or sneeze and people nearby breathe in these bacteria and become infected. Only 5–10 percent of infected but otherwise healthy people develop an active TB disease. Most people who carry the bacteria suffer no obvious symptoms and cannot pass on the disease to others during this latent phase of the infection. But if the immune system is weakened, active TB disease can occur. This occurs most in people infected with HIV/AIDS, which severely weakens the immune system.

The increased incidence of TB is a consequence of the spread of HIV/AIDS, the emergence of multi–drug resistant strains of TB and variability in protective efficacy of the only currently available vaccine, Bacillus Calmette–Guérin (BCG). Although the BCG vaccine offers protection against the most serious forms of TB in childhood, its efficacy wanes over a period of 10–15 years after the vaccination. A need for an alternative vaccination approach has emerged in the last two decades.

In March 2004 we announced a new collaboration with the Aeras Global TB Vaccine Foundation on the pre–clinical and clinical development of candidate tuberculosis (TB) vaccines. The Crucell–Aeras TB vaccine program will focus on improvement of BCG, using our PER.C6 and AdVac technologies. Aeras has agreed to provide us up to \$2.9 million contingent upon meeting certain development milestones, for development of TB vaccine candidates.

Rabies

Rabies is a viral disease of mammals most often transmitted through the bite of a rabid animal. The virus infects the central nervous system, causing encephalopathy and ultimately death if medical treatment is not sought before symptoms appear. Rabies is prevalent in all the continental regions of Europe, Asia, America and Africa. Greenland and countries in Eastern Europe also have rabies in their animal populations. Globally, approximately 10 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.

Post–exposure treatment for Rabies 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 recognised as being insufficient in quality and supply, as well as posing safety concerns because they originate from human or equine serum. Market opportunities for rabies treatments are projected to grow significantly as affected countries such as India and China grow in affluence.

We have developed a human monoclonal antibody product in collaboration with two leaders in the rabies antibody field, the Thomas Jefferson University (TJU) based in Philadelphia and the U.S. Centers for Disease Control and Prevention (CDC) in Atlanta, using MAbstract and PER.C6.

In experiments conducted during 2004 in collaboration with TJU and under a Collaborative Research and Development Agreement (CRADA) with the CDC, the antibody product demonstrated protection in the industry standard hamster model at least equivalent to HRIG.

Research to Improve Our Core Technologies to Maintain Our Competitive Position

To maintain our competitive position, in addition to the research and development we conduct as part of our everyday operations, we continually research improvements to and potential new versions of our core technologies. These efforts include the PER.C6 cell line, where we continually search for additional areas of application, MAbstract, AdVac and STAR. In the area of vaccines, we are working to identify viruses that can be grown using the PER.C6 technology, which could then be developed into vaccines. In addition to testing for additional applications of our existing PER.C6 technology, we are researching the creation of new cell lines from a variety of cell sources.

Other Collaborations and Agreements

Galapagos Genomics N.V.

Galapagos Genomics N.V. ("Galapagos") is a privately-held 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. Founded in Belgium in 1999 as a joint venture between IntroGene (Crucell's predecessor) and Tibotec-Virco (acquired by Jansen Pharmaceutica, a Johnson & Johnson company), it was established to put PER.C6 technology to use in the field of functional genomics. Research activities at Galapagos encompass internal programs in osteoporosis, rheumatoid arthritis, osteoarthritis and Alzheimer's disease, as well as numerous partnerships with pharmaceutical, nutraceutical and biotechnology companies. A newly established services unit, Galadeno, provides reagents and functional screens to such companies for the rapid identification and validation of novel drug targets. Partners of Galapagos include Bayer, Boehringer Ingelheim, Celgene, Johnson & Johnson, Organon, Pfizer, Procter & Gamble, Vertex and Wyeth.

Galapagos holds an exclusive license to 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. Tibotec and Crucell have agreed not to compete with the activities of Galapagos Genomics, which holds the rights to the products and technology that it develops.

Galapagos Genomics represents a financial investment for us, and we expect that we may sell our interest at some point in the future. Our current ownership has decreased to 20.8% as a result of private financing by Galapagos in 2002 that raised €23.4 million.

On March 9, 2005 we announced that Galapagos is considering a Euronext stock exchange listing in 2005. The primary reason for the listing is to raise additional funds to enhance Galapagos' drug discovery operations, which are predominantly aimed at developing breakthrough medicines for the bone and joint diseases osteoarthritis, osteoporosis and rheumatoid arthritis.

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 of product sales arising out of the collaborations. Generally, these collaborations specify that we provide the applicable university with a specific amount of funding, and in consideration of such, we receive certain intellectual property rights and access to the results of the university research.

Consulting Arrangements

We hire people with high-level experience in our fields of interest to provide advice and consulting services. We generally pay consultants on a per project basis and their term generally runs year-to-year. We require consultants, among other things, to adhere to confidentiality undertakings, and generally we have the right to all intellectual property created during the term of the consulting agreement.

Intellectual Property and Technology Licenses from Third Parties

Intellectual Property

Our success and ability to compete depends in large part on our ability to protect our proprietary technology and information, and to operate without infringing 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 United States and Europe, as well as in other jurisdictions as appropriate.

In addition to retaining outside patent counsel, we also employ European and Dutch patent attorneys that file, prosecute, defend and enforce patent rights as well as manage our patent portfolio. Our patent portfolio comprises 661 active cases (*i.e.* granted patents in force or pending patent applications) as of December 31, 2004. We aggressively protect our inventions and employ a proactive filing strategy with respect to patent applications. Our portfolio management involves active commercialization and enforcement strategies combined with disposal of cases that we no longer consider commercially attractive.

The following table reflects the total number of active cases (pending or granted) through December 31, 2004, 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. Patent filings classified under vaccines relate to AdVac-based and classical vaccines. Patent filings classified under antibodies relate to antibodies and/or drug targets, excluding the enabling technologies. Patent filings classified under technology primarily relate to cell-based production technology, adenoviral vector technology, STAR-technology and related technology, functional genomics and target and antibody discovery technology.

	Patent Filings		
	Pending	Granted	Total Active
Vaccines	155	104	259
Antibodies	70	22	92
Technology	131	71	202
Gene Therapy	53	55	108
Total	409	252	661

The following table summarizes the first filings for new inventions and the number of patents granted during 2004.

	First Filings and Granted Patents in 2004	
	First filings for new inventions	Granted patents
Vaccines	4	52
Antibodies	19	3
Technology	3	41
Gene Therapy	1	35
Total	27	131

Our new filings in the vaccine field in 2004 reflect our efforts to further strengthen our patent portfolio in support of product development programs in that area. The new filings in the area of antibodies reflect our intensified research and development in the field of infectious diseases and, to a lesser extent, the completion of development programs in the field of target and antibody discovery in oncology. 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. Since we are not actively involved in gene therapy research and development, only one new filing has been made in that area during 2004.

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 December 31, 2004, we have 96 pending applications in the EU,⁽¹⁾ 117 pending applications in the U.S.,⁽²⁾ 31 international patent applications (so-called "PCT"⁽³⁾ applications") and 165 applications in the rest of the world.⁽⁴⁾

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- (1) EU refers to filings made under the European patent convention. The EU figures do not include European patent applications designated in Patent Cooperation Treaty (PCT) applications while still in the international phase.
 - (2) U.S. figures do not include U.S. patent applications designated in PCT applications while still in the international phase.
 - (3) Figures reflect PCT applications still in the international phase. Our PCT applications routinely designate all territories and contracting states that are party to the Patent Cooperation Treaty per the international filing date.
 - (4) Rest of world consists of Australia, Brazil, Canada, China, India, Israel, Japan, Hong Kong, Mexico, New Zealand, Norway, Russia, Singapore, South Africa and South Korea. Rest of world figures do not include PCT-applications designating these countries while still in the international phase.

A significant number of our pending patent applications are filed under the Patent Cooperation Treaty (PCT), which offers a cost-effective method to seek provisional worldwide protection in more than 100 countries and territories for the duration of 30 or 31 months from the filing date. The decision to divide the PCT application into territories in which a granted patent is desired may be postponed until the obtainable scope of protection and the technical and commercial usefulness of the invention becomes clearer.

We currently own or co-own 164 granted patents in the EU territory, 29 patents in the U.S. and 59 patents in the rest of the world. During the pendency of a European patent application, a single application may designate 30 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.

Our patent-related activities do not afford complete protection to our intellectual property rights. Patents in the biotechnology and biopharmaceutical fields involve complex factual and legal questions. Patents may not be issued in respect of our pending applications or in respect of future applications that we file. In addition, 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. Our patent filings may be subject to interferences.

In 2004, a new regulation, the Technology Transfer Block Exemption Regulation, entered into force in the European Union, which may require us to review and possibly amend existing license and technology transfer agreements in the future to comply with the new regulation. This review process may be costly and time consuming and may require renegotiation of certain portions of our licenses and other agreements.

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. 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.

In October 2004 we commenced infringement litigation proceedings against CEVEC Pharmaceuticals in the District Court of Duesseldorf, Germany, arguing that CEVEC's cell line infringes a recently granted European patent for our PER.C6 technology. In December 2004 CEVEC

Pharmaceuticals acknowledged three out of four of our claims, but chose to defend the remaining claim. It is possible that the court will find against us on the remaining claim, and we cannot exclude the possibility that CEVEC will also file counterclaims in separate proceedings in order to attempt to have certain of our PER.C6 patents revoked or declared invalid.

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

Research has been conducted for many years in the fields of biotechnology and biopharmaceuticals. This has resulted in a substantial number of issued patents and an even larger number of patent applications. The patent office maintains patent applications filed only in the United States in secrecy until patents issue, and publication of patent applications elsewhere and of discoveries in the scientific or patent literature frequently occurs substantially later than the date of the underlying discoveries. Moreover, patents that appear not to affect our activities may be construed broadly. As such, we or our licensees may be found to infringe the patents or violate other proprietary rights of third parties and may be enjoined from pursuing research, development or commercialization of our or their products or be required to pay damages. In these circumstances, licensing or other arrangements for addressing these infringements or violations may not be available, or may not be available on commercially acceptable terms.

When licensing our technology to third parties we seek to obtain access to any improvement patents 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 from Third Parties

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

In 2003 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 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 to phage antibody-display technology and part human, or chimeric, binding proteins and molecules from Enzon Corporation's subsidiary, SCA Ventures, Inc.

We also have exclusive licenses or an option for an exclusive license to a number of genes, which we may use in the development of products in the area of gene therapy. In some cases we will be required to make royalty payments in the event of product sales based on these genes.

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

Seasonality

Our revenues are related to specific license agreements and can therefore vary materially from quarter to quarter. Our revenues were highest during the second quarter of 2004. We do not believe there is any specific seasonal pattern to our license or government grant revenues.

Regulation

We operate in a highly regulated industry. Our activities involve the use of hazardous materials, including chemicals and radioactive and biological materials, and animal testing, all of which are subject to regulation. 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.

Our ability and that of our licensees to commercially distribute biopharmaceuticals depends in part on the extent to which governmental health administration authorities, health maintenance organizations, or HMOs, and other organizations are willing to pay for the costs of these products. The willingness of governments and HMOs to pay for the costs of newly developed health care products is uncertain. There are efforts by governmental payers and HMOs to contain or reduce the costs of health care and we expect that there will continue to be a number of legislative proposals to do so.

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 our licensees or we develop will require regulatory clearances prior to clinical trials and additional regulatory clearances prior to being produced and distributed commercially. These regulatory processes are generally stringent and time-consuming. We expect the European Medicines Agency (EMA) in Europe, the Food & Drug Administration (FDA) in the United States, the *College ter Beoordeling van Geneesmiddelen* (CBG) in The Netherlands and comparable agencies in other countries to subject new biopharmaceutical products to extensive regulation. These regulatory requirements with which our licensees and we will have to comply will evolve over time due to the novelty of the biopharmaceutical products and therapies currently under development. Fortunately, the harmonization of these requirements is promoted at an international level (International Conferences on Harmonization (ICH)) to avoid unnecessary repetition of studies when seeking approval in various countries. Under the current definitions, we believe that products developed using our technologies will be regulated either as biological products or as drugs.

Before marketing a (bio)pharmaceutical product, companies require regulatory approval from the relevant authorities. To obtain this approval, pre-clinical animal studies and human 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 animal 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 EMA in Europe, the FDA in the United States 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 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 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.

Europe

There is a broad range of legislation in force in member states of the EU governing the testing, manufacturing and marketing of biopharmaceutical products, both at an individual as well as a central level (European Commission Directives). This legislation imposes specific requirements on various topics including pre-clinical and clinical testing and the operation of laboratories and manufacturing sites. Furthermore, there are specific directives and other legislation on, among other things, pricing, distribution, labeling and advertising of medicinal products.

At the central level, legislation on medicinal products was first enacted in Directive 65/65/EEC: "on the approximation of provisions laid down by law, regulation or administrative action relating to medicinal products". Subsequent Directives (75/318/EEC, 75/319/EEC and 93/39/EEC) have further amended and expanded the original provisions, resulting in a system for the regulation of drugs, or medicinal products as they are called in the EU, based on the principle of mutual recognition. Under this mutual recognition procedure, the applicant first submits its product for review to one or more EU member states. The first member state that decides to evaluate the product is called the reference member state. After the reference member state has assessed the medicinal product for quality, safety, and efficacy and has granted a national marketing authorization, other member states that have received copies of the application have 90 days for evaluation before they must grant authorization as well. In case of refusal, the application will be sent to the Committee for Human Medicinal Products (CHMP) for arbitration.

An alternative, centralized, approach for registration has been provided by Directive 93/41/EEC and Council Regulation No 2309/93, which lay down EU procedures for the authorization and supervision of medicinal products for human and veterinary use and establish a European Medicines Agency (EMA). Under this centralized procedure, which has been implemented for so-called high technology medicinal products, particularly those derived from biotechnological processes, applicants submit their dossier for authorization to the EMA. The EMA coordinates the assessment process by appointing two EU member states as a rapporteur and co-rapporteur, respectively, who will assess the application and prepare draft reports for review by the CHMP. The CHMP issues an opinion on the product's quality, safety and efficacy and sends its opinion to the European Commission, which drafts a decision based on that opinion. After consulting with its standing committee, the European Commission may grant a marketing authorization, subject to adequate evidence of quality, safety and efficacy. The marketing authorization granted is valid in all EU member states.

Since May 1, 2004, the Clinical Trial Directive (2001/20/EC) has come into effect. The aim of this directive is to harmonize the process for authorization and conduct of clinical trials as it is implemented in the individual EU member states. As a result of Directive 2001/20/EC, the GMP requirements for the manufacture of investigational drugs have been changed, and a specific requirement for product release by a Qualified Person has been included in the requirements. Also,

regulatory inspections of manufacturing facilities for investigated drugs have been made obligatory, where in the past this was on a voluntary basis in most European countries. Manufacturers of pharmaceutical products operating within the EU must hold a manufacturer's authorization and must comply with the requirements of good manufacturing practice (GMP) incorporated into EU legislation (2003/94/EC). We have already obtained a GMP manufacturing license for our pilot facilities, and we also employ two Qualified Persons for production releases. These requirements are intended to set minimum standards with respect to manufacturing facilities and the way of operating these facilities. Failure to comply with these requirements may result in the suspension or revocation of the manufacturer's manufacturing authorization.

United States

The Federal Food, Drug and Cosmetic Act regulates both drugs and biological products, and the Public Health Service Act also regulates biological products. The areas that these two Acts and related regulations govern include testing, manufacturing, safety, efficacy, labeling, storage, record keeping and advertising and other promotional practices. The FDA must approve a product or provide alternative clearances before clinical testing or manufacturing and marketing of biologics or drugs may begin.

In order to gain FDA approval to conduct clinical trials, pre-clinical studies must generally be conducted in the laboratory and in animal model systems to gain preliminary information on an agent's efficacy and to identify any major safety concerns. Applicants submit the results of these studies, in addition to information regarding the manufacture of the medicinal product, as a part of an application for an Investigational New Drug, or IND. Furthermore, the IND application includes a detailed description of the clinical investigations.

The clinical studies are designed to demonstrate the safety and efficacy of the new drug. The FDA receives reports on the progress of each phase of clinical testing, and it may require the modification, suspension, or termination of clinical trials if an unwarranted risk is presented to patients. Recently, the FDA has issued the so-called "two animal rule." According to this rule, extensive clinical trials in humans intended to demonstrate efficacy may not be necessary when it is impractical or unethical to perform efficacy trials. Instead, the efficacy must be demonstrated in relevant animal models, while safety trials in human volunteers will continue to be required.

After all studies and trials of a new product have been completed, applicants must submit all data to the FDA for review in order to obtain marketing approval. If the product is regulated as a biologic, applicants must submit a Biologic License Application, or BLA. If the product is classified as a new drug, a New Drug Application, or NDA is required. The NDA or BLA must include results of product development activities, pre-clinical studies and clinical trials in addition to detailed manufacturing information.

The FDA subjects NDAs or BLAs to a detailed and potentially time-consuming approval process. The FDA may ultimately decide that the application does not satisfy its criteria for approval or may require additional pre-clinical or clinical studies. Even if applicants obtain FDA regulatory clearances, the FDA subjects a marketed product to continual review, and subsequent discovery of previously unknown problems or failure to comply with the applicable regulatory requirements may result in restrictions on the marketing of a product or mandated withdrawal of the product from the market as well as possible civil or criminal sanctions. Before marketing clearance is secured, the manufacturing facility will be inspected for compliance with current Good Manufacturing Practices requirements by FDA inspectors and will be inspected periodically for continuing compliance by FDA inspectors.

In addition to the FDA requirements, the NIH has established guidelines for research involving recombinant DNA molecules. These guidelines apply to all recombinant DNA research that the NIH conducts or supports, including proposals to conduct clinical research involving DNA therapeutics, including our collaboration with the NIH to develop Ebola and malaria vaccines. The NIH review of

clinical trial proposals is a public process and usually involves review and approval by the Recombinant DNA Advisory Committee of the NIH.

Biologics Master File. The PER.C6 cell substrate Biologics Master File (BMF) is the regulatory dossier filed with the FDA in the United States, which describes various aspects of our PER.C6 technology. We have submitted a Biologics Master File (BMF) to the FDA. The companies to which we license our PER.C6 technology can take advantage of the BMF that we have filed with the FDA and need not compile their own history of the PER.C6 cell line when they seek regulatory approval of any biopharmaceutical product that they may produce using it. This may assist our licensees in applications they may make to the FDA for products manufactured using the PER.C6 technology. We are required by regulators to supplement our BMF when new information arises.

During 2003, we expanded our cooperation agreement made with Merck & Co., Inc., which relates to the PER.C6 cell substrate Biologics Master File in the U.S., and equivalent authorities in other jurisdictions. Under the terms of the agreement, we agreed to work closely with Merck on matters relevant to maintenance of the PER.C6 cell substrate BMF, including the provision of technical assistance and guidance from Merck as appropriate.

Competition

The field of biotechnology 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 also may experience competition from companies that have acquired or may acquire technology from universities and 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.

Vaccines

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 MDCK (Madin Darby Canine Kidney cells) and VERO (monkey cells) 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 also aware of other human expression technologies such as WI-38 and MRC-5 for licensed and marketed vaccines, as well as human cell lines supporting products in development such as (HEK)-293. Other biotechnology and pharmaceutical companies that are focused on developing vaccines against infectious diseases include Wyeth, sanofi pasteur, Merck & Co., Chiron, Acambis, Baxter, GenVec, Berna Biotech, Bavarian Nordic, Baxter, Solvay, Shire, Vical and Nobilon.

In the area of influenza, we are aware that Solvay has obtained registration in The Netherlands for a vaccine based on MDCK cells. We are aware of other biotechnology and pharmaceutical companies that currently are developing influenza vaccines based on MDCK cells, including Shire and Chiron. In addition, we are aware that Baxter has obtained approval in Austria for its VERO-based influenza vaccine. For other European markets Baxter appears to have stopped at Phase II in December 2004.

In the area of West Nile virus, we are aware that Acambis is conducting a Phase I clinical safety study in humans with its West Nile ChimeriVax vaccine. This vaccine uses a genetically engineered yellow fever 17D live virus containing the genes encoding the antigens responsible for protection

against West Nile virus. We also are aware that Vical is developing a DNA-based West Nile virus vaccine that uses portions of the genetic code of a pathogen to cause the host to produce specific features of the pathogen that may induce an immune response. This method could potentially offer superior safety, ease and reliability of manufacturing, as well as storage and handling advantages, compared with conventional vaccines that use live, weakened or dead pathogens to produce an immune response. In addition, other parties are working on human West Nile virus vaccine research. The University of Queensland is working on a vaccine based on the relatively harmless Kunjin virus, a flavivirus found in Australia, and Hawaii Biotech received significant funding from the NIH in December 2004 in support of the pre-clinical development of its West Nile vaccine candidate.

In the area of Ebola, we are aware that Vical is conducting Phase I clinical efficacy studies with its DNA-based Ebola vaccine and has initiated GMP manufacturing for the NIH with whom they are jointly developing the vaccine. We are aware that Health Canada, a federal government organization, is conducting pre-clinical studies with its Ebola vaccine that is based on a live replication competent Vesicular Stomatitis Virus (VSV) vector. We are also aware that the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID) is conducting pre-clinical studies with its recombinant Ebola vaccine, which is based on Ebola virus-like-particle (VLP) technology. USAMRIID is also involved in a CRADA with AVI BioPharma in testing the latter's antisense drugs against Ebola. AVI BioPharma received funding from the U.S. Senate Committee on Appropriations in June 2004 to support this and its work on Marburg virus.

In the area of malaria, we are aware of two companies conducting Phase I/II clinical studies with malaria vaccine candidates based on virus-like-particle (VLP) technology: GlaxoSmithKline Biologicals (GSK) and Apovia. We are also aware that Oxford (The Wellcome Trust Centre for Human Genetics) and GSK are jointly developing a malaria vaccine using live vector technology, and that this vaccine is in Phase I/II a clinical studies. In addition, Oxford is conducting Phase I/II clinical studies with three additional malaria vaccine candidates based on live vector technology, as well as pre-clinical studies with one additional vaccine candidate based on live vector technology. We are aware that the Pasteur Institute is conducting Phase I/IIa clinical studies with its malaria vaccine candidate, which is based on Long Synthetic peptide technology (LSA-3).

For tuberculosis, a number of companies, government bodies and academic institutes around the world are working on the development of new vaccines. The NIAID in the U.S. is involved in a range of early-stage efforts relating to live-attenuated, subunit and naked DNA type vaccine candidates. Our partner, the Aeras Global TB Vaccine Foundation, is working on various other programs including a live recombinant TB vaccine with the David Geffen School of Medicine at UCLA, which entered its first clinical trial in March 2004. In October *Nature Medicine* announced an Oxford University subunit vaccine, designed to work in tandem with the existing BCG vaccine, had successfully completed safety trials with positive T-cell responses.

Antibodies

Other biotechnology companies, including Celltech Group plc and Protein Design Laboratories, Inc., currently generate humanized antibodies, and Medarex, Inc. and Abgenix Corp. produce fully-human antibodies from transgenic mice. MorphoSys AG and Cambridge Antibody Technology Group plc generate fully-human antibodies using phage antibody-display libraries that are similar to ours. Companies such as Dyax Corp., 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 Chiron and Baxter, and monoclonal antibody companies like Neutec Pharma, MedImmune, XTL Bio, Inhibitex and Biosynexis. For rabies specifically, Crucell's antibody product may

offer an alternative to the existing Rabies Immune Globulin products, both Human (HRIG) and Equine (HRIG), that are currently paired with rabies vaccine for effective post-exposure treatment.

Production of Recombinant Proteins and Monoclonal Antibodies

Other companies use cell lines derived from animals. Chinese hamster ovary (CHO) and murine myeloma (NS0) cells are widely used for the development and/or commercial production of monoclonal antibodies and other recombinant proteins by companies including Genentech, Biogen, Centocor, Amgen, Lonza and Boehringer Ingelheim.

We are aware of a human cell-line expression platform used for production of recombinant proteins, the 293 human cell-line, which shares some of the advantages of the PER.C6 cell line. The 293 human cell line is utilized by Eli Lilly & Company to produce a protein for the treatment of adult severe sepsis. The FDA and the EMEA have approved this product and it is currently available for use. We are aware that scientists have published research describing human cell culture systems that appear to have similarities to our PER.C6 cell line.

Adenoviral Vector Technology and other Recombinant Vectors

With respect to vector development, we are aware of several competing technologies, including those of GenVec and Merck & Co., which may pose a threat to the commercial viability of our AdVac technology. In particular, Merck & Co. research has established methods that may prevent problems relating to pre-existing immunity to adenovirus 5 vectors. If successful, these methods may limit the development of a market for our AdVac technology.

Property, Plant and Equipment

Our research activities and corporate offices are located in facilities of approximately 7,800 square meters in Leiden, The Netherlands. We sub-lease 1,000 square meters of this space to Pharming Technologies B.V. and 500 square meters to Galapagos Genomics. In addition, we lease 770 square meters of space adjacent to these corporate offices, of which 439 square meters is subleased to a third party. Our plant and production facilities are located in a separate building in the Leiden BioScience Park, including 265 square meters of production space, 75 square meters of quality-control laboratories and 228 square meters of office space.

The section of the main building that we use includes 2,100 square meters of laboratories, with BioSafety Level (BSL) 1, BSL 2 and BSL 3 labs, including an animal facility. The remainder of the main building is divided into 2,800 square meters of office space and 1,400 square meters for storage, technical areas, washrooms, waste destruction and sterilization.

Insurance

We have in place general third party public and product liability insurance. Our policy would not cover any of our activities domiciled in the United States or Canada, has a limit of liability and has certain additional conditions to coverage and deductibles. We do not insure our phage antibody-display library or PER.C6 master cell bank, though identical copies of the same cell bank are stored in multiple locations in Europe. We carry insurance relating to theft, fire and damage to the moveable assets within our facilities and other customary insurance coverage for most of our activities, including liability insurance coverage for the management board, management committee and the supervisory board.

Sales and Business Development

We currently employ seven people in our sales and business development operations. Our business development strategy has historically involved contacting prospective licensees, assessing their interest in our technologies, and, if the prospective licensee indicates interest, negotiating a license and/or collaboration agreement pursuant to which we deliver the applicable technology to, or collaborate with, the licensee. For some of our contracts we provide services, for which we are paid at different rates. To support our licensing activities we at times provide our technology for free for a short term evaluation by the licensee, or provide contract service activities prior to providing a license, such as generation of an antibody production clone or production of adenoviral vectors.

Item 5. Operating and Financial Review and Prospects

The following discussion contains forward-looking statements based upon current expectations that involve risks and uncertainties. When used in this annual report, the words "intend", "anticipate", "believe", "estimate", "plan", and "expect" and similar expressions as they relate to us are included to identify forward-looking statements. Our actual results and the timing of certain events could differ materially from those anticipated in these forward-looking statements as a result of certain factors, including those set forth below and elsewhere in this annual report. See "Forward-looking Statements" and Item 3, "Key Information—Risk Factors." You should read the following discussion in conjunction with our consolidated financial statements and the notes thereto, which we have included elsewhere in this annual report.

All amounts in this Item 5 are in thousands of euro, except share and option data.

Operating results

Overview

General

We are a biotechnology company that combines proprietary technologies to discover, develop and produce a variety of biological products for the prevention and treatment of infectious diseases. Unlike the technologies generally employed in our industry, our technologies enable the development and production of biological products that may overcome the limitations inherent in many currently available products. We face a variety of challenges and opportunities in bringing our products to market and responding to the dynamics of the biotechnology industry, which is characterized by rapid change and intense competition. Our strategy revolves around continued investment in research and product development, particularly related to infectious diseases, expanding the portfolio of licensees using our proprietary technology, partnering with global industry leaders, and working to improve our operating results and financial strength. Our financial strength and ability to adapt to the current market and economic conditions are dependent, in part, on the cost of bringing novel vaccines to market in our chosen field, the success of our licensees in developing commercial products using our technology, and effective management of our working capital.

We generate revenue and cash flow primarily through the licensing of our proprietary technology. In areas where we are not developing our own products, we offer our PER.C6 technology to the biopharmaceutical industry for the development and production of diverse biopharmaceutical products. Within our chosen areas of focus, we sometimes collaborate with leading biopharmaceutical manufacturers to develop products or processes.

In 2004, our revenues increased to €22,622 from €7,424 in 2003 and €9,575 in 2002. During this period, our total headcount increased from 183 to 210 employees on a full-time basis. At December 31, 2004, 171 of our 210 full time equivalent employees were engaged in, or directly supported, research and development activities.

Our total cost and expenses were €68,231 in 2002, €33,916 in 2003 and €45,348 in 2004. These amounts included non-cash charges of: €33,593 in 2002 related to developed technology amortization, goodwill impairment and stock option compensation; and €4,026 and €4,532 related to developed technology amortization and stock option compensation in 2003 and 2004, respectively. We incurred a loss from operations of €22,726 in 2004 as compared to an operating loss of €26,492 in 2003. At December 31, 2004, our accumulated deficit was €274,524 and our total shareholders' equity was €78,535. Although we do not expect to significantly expand our research and development activities or corporate infrastructure levels in the near future, we expect to continue to incur operating and net losses over at least the next several years.

With the discussion of our financial condition and results of operations that follows, we intend to provide information that will assist in understanding our financial statements, the changes in certain key items in those financial statements from year to year, and the primary factors that accounted for those changes, as well as how certain accounting principles, policies and estimates affect our financial statements.

Critical Accounting Policies

The methods, estimates and judgments we use in applying our most critical accounting policies have a significant impact on the results we report in our financial statements. The U.S. Securities and Exchange Commission has defined the most critical accounting policies as the ones that are most important to the portrayal of our financial condition and results, and requires us to make difficult and subjective judgments, often as a result of the need to make estimates of matters that are inherently uncertain. Based on this definition, our most critical policies include revenue recognition, the assessment of recoverability of our intangible assets, which impacts the valuation of intangible assets, and the determination of the fair value of stock-based compensation, which impacts compensation expense. Below we discuss these policies further, as well as the estimates and judgments involved. The development and selection of our critical accounting estimates have been discussed by management with our audit committee.

Revenue and Revenue Recognition

Licensing our PER.C6 technology to third parties is a key element of our strategy to establish PER.C6 as the cell-line of choice in the biopharmaceutical industry. Our license agreements generally provide for a non-refundable payment upon signing, a non-refundable fixed annual or fixed semi-annual payment (which is generally creditable against future royalty payments) payable in arrears and royalty payments calculated as a percentage of the net sales of the licensee using our technology. The payment upon signing under these license agreements is generally larger than the subsequent annual or semi-annual payments. Certain license agreements provide for additional non-refundable license fees to be paid upon the achievement of contractually defined milestones.

We also aim to generate revenues in the future from the commercial distribution of biopharmaceutical products developed using our core technologies. We intend to market our own products through collaborations or strategic alliances with third parties, particularly pharmaceutical and biopharmaceutical companies. The timing and nature of these arrangements will depend on a number of factors, including the product's likelihood of clinical success, its stage of development, its commercial potential and the resources and abilities of our prospective partner.

We earn revenues from government grants received from the Dutch government and the European Union. We expect to continue to generate revenues from such government grants in the future. We have also filed grant proposals and expect to generate additional revenues from grants from non-governmental, semi-governmental and governmental bodies in the United States. Grants generally take the form of reimbursements for specific expenses incurred in connection with approved scientific research activities. We intend to continue to apply for available public grants and non-governmental organization support in the future, though the timing and amount of any grant revenues are uncertain. We recognize revenues from grants when we incur the related expenses and collectibility of the grant is probable.

We recognize initial fees related to the licensing of our technology as revenues over the period of our significant continuing performance obligations, if any, and upon persuasive evidence of an arrangement and delivery of the associated technology. Under certain arrangements, we have no continuing performance obligations after delivery of the associated technology under the license agreement or any other arrangement with the licensee. In such arrangements, the initial license fees

recognized as revenue relate to the complete transfer of our fully developed technology to the licensee and represent the culmination of the earnings process.

While for the majority of our license agreements we have no significant continuing performance obligations subsequent to the delivery of the associated technology, in certain arrangements we collaborate with a licensee to achieve certain specified results. Under these agreements, we have significant continuing performance obligations related to research and development subsequent to the delivery of the licensed technology. We recognize non-refundable up-front payments as revenue over the expected period of our significant continuing involvement, the term of which is consistent with our development plans. Our two most significant collaboration agreements are with DSM Biologics and sanofi pasteur. In 2003, we recognized revenue of €1,250 related to our arrangement with DSM and no revenue related to our arrangement with sanofi pasteur. In 2004, we recognized revenue of €5,250 related to our arrangement with DSM and €5,792 related to our arrangement with sanofi pasteur.

Certain of our license arrangements provide for additional non-refundable license fees to be paid upon the achievement of milestones. We recognize such additional license fees as revenue when the amounts become due and payable.

In addition to the initial fee, our arrangements generally provide that the licensees make semi-annual or annual payments ("license maintenance fees") to maintain the license for a subsequent term. Generally, licensees may terminate the license and related maintenance fees upon 30 days' to 90 days' notice. We recognize annual and semi-annual non-refundable license maintenance fees as revenues when the amounts become fixed and payable. The aggregate of annual or semi-annual license maintenance fees paid generally will reduce any royalty payments which may be due based on future product sales of the licensee, if any, under the license agreement. Although we have not received royalty payments from our licensees to date, we will recognize royalties as revenue when they become fixed and payable, to the extent we receive such royalties in the future.

As part of various collaboration agreements, we receive service fees for work performed under such agreements.

Intangible Assets

We perform tests for impairment of intangible assets whenever events or circumstances suggest the value of such assets may be impaired. At December 31, 2004, our intangible assets consisted entirely of developed technology with a net carrying value of €4,047. To evaluate potential impairment of developed technology, we assess whether the future cash flows related to the asset will be greater than its current carrying value. Accordingly, while our cash flow assumptions are consistent with the plans and estimates we are using to manage the underlying business, there is significant judgment in determining the cash flows attributable to our developed technology over its estimated useful life. However, a reduction of the projected annual cash flows attributable to our developed technology of up to 50% would still not have resulted in an impairment charge.

Stock-Based Compensation

We account for employee stock-based compensation in accordance with the fair value method under Statement of Financial Accounting Standard No. 123, "Accounting for Stock-Based Compensation" and we account for non-employee stock-based compensation in accordance with Emerging Issues Task Force No. 96-18, "Accounting for Equity Instruments That Are Issued to Other Than Employees for Acquiring, or in Conjunction with Selling, Goods or Services." We value our stock options and stock warrants using the Black-Scholes and Bloomberg pricing models which requires us to make several key judgments including: the expected life of issued stock options, the expected volatility of our stock price, and the expected dividend yield to be realized over the life of the stock option or stock warrant. These estimates have been prepared based upon our historical experience and our best

estimation of the future. Changing any of the above assumptions, particularly the expected volatility of our stock price or the expected life of our stock options, would have a significant impact on the amount of compensation expense recognized.

Results of Operations

Years Ended December 31, 2002, 2003 and 2004

Revenues

The following table shows our revenues for each of the years in the three-year period ended December 31, 2004, and the percentage changes between these periods.

	Year ended December 31,			% change 2002-2003	% change 2003-2004
	2002	2003	2004		
License revenues	€6,664	€4,800	€12,429	(28.0)	158.9
Service fees	—	404	5,712	100.0	1,313.9
Government grants and other revenue	2,911	2,220	4,481	(23.7)	101.8
Total revenues	€9,575	€7,424	€22,622	(22.5)	204.7

Our total revenues increased by 204.7% in 2004 compared with 2003, and decreased by 22.5% in 2003 compared with 2002. In 2004, the increase in total revenues compared to 2003 is primarily due to an increase in license revenues from new and existing contracts of €7,629 or 158.9%, an increase in service fees for collaboration agreements of €5,308 and an increase in government grant and other revenues of €2,261 or 101.8%. The decrease in 2003 compared to 2002 was primarily due to a decrease in license revenues of €1,864 or 28.0%. The decrease in license revenue was principally due to a decrease in initial license fees from new license arrangements in 2003 and, to a lesser extent, existing licensees electing not to continue their license arrangement. In 2004, we recognized revenue of €3,886 from twenty new PER.C6 license arrangements versus €587 from ten new PER.C6 license arrangements in 2003. Also, a significant initial license fee from an arrangement we entered into with sanofi pasteur in 2003 was not recognized as revenue, but is deferred and will be recognized as revenue over three years, the period of our expected continuing involvement. During 2003, existing licenses with Cell Genesys, Inc., NatImmune A/S, Novavax, Pfizer, Inc., and Schering AG were terminated. In the aggregate, annual payments from these license arrangements and options amount to €536.

Revenues generated from government grants and other revenue increased 101.8% in 2004 to €4,481 after a decrease of 23.7% in 2003. The increase in 2004 is primarily a result of additional subsidies that were granted by the Dutch government and additional revenues recognized from our services. The decrease in 2003, amounting to €691, was primarily a result of a decreased level of production fees received in connection with our production facility, and lower reimbursable research and development expenses. Total fees recognized as revenues in connection with our production facility in 2004 and 2003 were €1,040 and €235, respectively.

In the past, we have experienced significant fluctuations in quarterly revenues and expects to continue to experience such fluctuations in the future.

Costs and Expenses

The following table shows our costs and expenses for each of the years in the three-year period ended December 31, 2004, and the percentage change between these periods.

	Year ended December 31,			% change 2002–2003	% change 2003–2004
	2002	2003	2004		
Cost of service fees	€ —	€ 399	€ 5,644	100	1,314.5
Research and development	24,252	21,885	20,468	(9.8)	(6.5)
Selling, general and administrative	10,386	7,606	14,704	(26.8)	93.3
Developed technology amortization	1,331	1,330	1,966	—	47.8
Goodwill impairment	30,891	—	—	(100.0)	—
Stock-based employee compensation	1,371	2,696	2,566	96.6	(4.8)
Total costs and expenses	€68,231	€33,916	€45,348	(50.3)	33.7

Research and Development Expenses. In 2004, research and development expense represented 45.1% of our total costs and expenses. We expect that our expenses will continue to consist principally of research and development expenses, primarily to support development of our technology platforms and research on potential products based on these platforms. Research and development expenses consist primarily of salaries and other personnel-related expenses for research and development personnel, laboratory expenses, technology purchases, patent related fees, technology license fees, depreciation and amortization of tangible assets related to research and development, and lease expenses. Research and development expenses also include fees we pay to third parties who conduct research on our behalf.

Research and development expenses decreased by 6.5% in 2004 compared with 2003 after a decrease of 9.8% in 2003 compared with 2002. The decrease in 2004 was due to an increase in the allocation of research and development related expenses to cost of service fees. The number of research and development employees increased from 151 at the end of 2003 to 169 at the end of 2004.

The decrease in 2003 was partially due to a decrease in our number of full-time employees engaged in research and development during 2003 from 154 at the end of 2002 to 151 at the end of 2003. During 2002 we had a maximum of 196 full-time employees, which resulted in a significant increase in laboratory expenses. In addition, fees paid for research and development performed by third parties decreased from €2,300 in 2002 compared to €1,794 in 2003. Finally, the decrease of research and development activities in 2003 compared to 2002 was due to changes made to our overall compensation programs and severance benefits paid to employees in 2002, including a severance payment of €650 to our former Chief Scientific Officer.

Selling, General and Administrative Expenses. Selling, general and administrative expenses consist primarily of salaries and other personnel-related expenses for personnel in the area of finance, human resources, business development, investor relations, legal and general management, costs of professional services (such as financial, legal, and accounting) and lease expenses.

In 2004, selling, general and administrative expenses were €14,704, an increase of 93.3% compared to €7,606 in 2003. This increase was primarily driven by increases in non-cash expenses of €4,800. Non-cash expenses consisted of a €3,100 increase in warrant expenses as a result of share price increases, and a €1,700 non-cash increase in compensation expense. This is related to a one-time, non-cash reduction of compensation expenses in 2003. The remaining €2,300 increase in selling, general and administrative expenses was mainly due to increases in insurance premiums, advisory costs and compensation expenses over the year.

Selling, general and administrative expenses decreased by 26.8% in 2003 compared with 2002. The decrease in 2003 was primarily due to changes in our overall compensation programs and, to a lesser extent, continued focus on operational cost control. In addition to employee salaries, our compensation program includes the issuance of options to employees as a means of attracting and retaining talented personnel. As described in Note 6 to our financial statements, our stock option plan provides for the issuance of stock options with an exercise price that exceeds the fair value of our ordinary shares on the date of grant. Under the terms of a cash bonus plan, if an employee maintains continuous employment with us for a period of four to five years and exercises the option in the last month of the option term, the employee receives a cash bonus. We recognize compensation expense ratably during the employment period required under the cash bonus plan.

In January 2003, the supervisory board approved a stock option plan whereby employees previously awarded options with an exercise price of €21.00 were able to exchange such options for an equal number of new options with an exercise price of €3.49. In conjunction with the replacement of these options, participating employees forfeited their right to receive the cash bonus related to the €21.00 option award. Accordingly, the Company recorded a reduction to compensation expense of €2,300 related to the forfeited cash bonus awards. This reduction to compensation expense is one-time, non-cash charge and is not indicative of operational changes that will benefit future periods.

In April 2004, the supervisory board approved a new option plan whereby employees and supervisory board are granted options with an exercise price 126% greater than the average closing stock price of the Company on the three days preceding the option grant date and have a five year life. The options are subject to profit retribution provisions. Such provisions entitle the Company to receive a portion of the profits upon the sale of the shares, calculated as the difference between the total proceeds from the sale of shares, and the aggregate selling price. The portion of the profits payable to the Company decreases ratably over three years. The relevant portion of any profits derived by the employee from the sale of shares received on exercise of options must be remitted to the Company if the employee terminates employment prior to the end of the three-year period.

Developed Technology Amortization. Amortization of developed technology was €1,966 and €1,330 in 2004 and 2003, respectively. In 2004, the amortization relates to developed technology acquired in 2004 and acquired in connection with a business combination in June 2000. The amortization in 2003 only relates to developed technology acquired in 2000. We amortize the developed technology using the straight-line method over a 5-year period. The carrying value per December 31, 2004 is €3,381 for the developed technology acquired in 2004 and €666 for the developed technology acquired in 2000.

Goodwill Amortization and Goodwill Impairment. Beginning January 1, 2002, upon the adoption of SFAS No. 142, we ceased amortizing goodwill on a straight-line basis and began subjecting goodwill to annual impairment tests. We performed the first annual impairment test at the end of 2002 and determined the full amount of our goodwill of €30,891 was impaired and the amount was charged to operations.

Stock-based Employee Compensation. Stock-based employee compensation decreased to €2,566 in 2004 from €2,696 in 2003 after an increase compared to €1,371 in 2002. The increase in 2003 compared to 2002 was primarily due to the issuance of 2,512,554 options during the year and changes made to the terms of all outstanding stock options to supervisory board members such that the options vest immediately and are no longer subject to profit retribution provisions. Accordingly, we recognized compensation expense of €495 representing the total amount of deferred compensation associated with options held by members of the supervisory board.

Interest Income

The following table shows our net interest income for each of the years in the three-year period ended December 31, 2004, and the percentage change between these periods.

	Year ended December 31,			% change 2002–2003	% change 2003–2004
	2002	2003	2004		
Interest income, net	€3,547	€2,143	€1,503	(39.6)%	(29.9)%

Net interest income decreased 29.9% in 2004 compared with 2003 and decreased 39.6% in 2003 compared with 2002. The decreases in 2004 and 2003 are primarily the result of lower average interest yields on available cash balances and lower cash balances due to the funding of operations.

Interest expenses relating to capital lease contracts are included in the foregoing. Those expenses amounted to €221 in 2003 and €212 in 2004.

Equity in Losses of Unconsolidated Investments

We incurred a net loss of €507 in 2002, representing our share of the net losses of Galapagos Genomics. During 2002 our proportional share of the losses of Galapagos Genomics reduced the carrying amount of our investment to zero and therefore no equity losses were recognized in 2003 and 2004.

Liquidity and Capital Resources

As of December 31, 2004, we had €76,711 in cash and cash equivalents.

To date, we have financed our operations primarily through equity issuances (including exercises under stock-based compensation plans). Since our initial public offering in 2000, which generated net proceeds of €128,003, proceeds from equity issuances amounted to €3,149, including €1,409 in 2004. In 2004, 2003 and 2002, we received proceeds of €741, €1,258 and €5,349, respectively, from sale and leaseback transactions.

We made capital investments in plant and equipment of €2,972 in 2002, €3,448 in 2003 and €2,114 in 2004. In 2003, we received proceeds of €1,306 from the sale of available-for-sale securities, which were received in exchange for services rendered. We do not maintain any available for sale securities as of December 31, 2004.

In 2004 we acquired the outstanding capital stock of ChromaGenics B.V., a privately held biotechnology company based in Amsterdam, the Netherlands. The acquisition has been accounted for as an acquisition of developed technology. We paid €4,017 in cash as well as entered into a contingent payment agreement that could result in an additional payment of €7,000 upon our receipt of revenues generated from the STAR technology. After the payments of the contingent consideration, we will pay a royalty on revenues generated from the STAR technology through the date the STAR technology patent expires.

Our cash flow from financing activities decreased from €5,874 in 2002 to €666 in 2003 and increased to €1,018 in 2004. The decrease in 2003 was primarily due to a decrease in proceeds from sale and leaseback transactions of €4,091 to €1,258. The increase in 2004 was primarily a result of additional proceeds from the issuance of ordinary shares that resulted from the exercise of employee stock options. We do not expect to generate significant cash proceeds from sale and leaseback transactions in the future. In 2003 and 2004, we made principle payments under capital lease obligations of €902 and €1,132, respectively.

We expect to continue to make investments in plant and equipment as required by our development programs. Investments in plant and equipment will be mainly financed through capital

leases, and is not expected to impact our burn rate significantly. We may use a portion of our cash to acquire or invest in complementary businesses, products or technologies, or to license—in the right to use such complementary technologies. We believe our current cash balances and operating revenues will be sufficient to satisfy our anticipated cash needs for working capital and capital expenditures for at least the next 24 months. However, it is possible that we will seek additional financing within this timeframe. We may raise additional funds through public or private financing, strategic alliances or other arrangements. We may not be able to raise additional funding. Further, any additional equity financing will be dilutive to shareholders, and debt financing, if available, may involve restrictive covenants. Our failure to raise capital when needed will harm our business and operating results.

Certain of our lease agreements contain provisions whereby we are required to make immediate payment of all amounts due under the lease in the event our cash and cash equivalents balance falls below €25,000 or our stockholders' equity or our cash and cash equivalents balance falls below €75,000. At December 31, 2004, €3,880 of amounts due under leases are subject to this provision.

Taxation

We have to date incurred net losses and, accordingly, have not paid corporate income taxes. The current corporate income tax rate in The Netherlands is 34.5%. A special 29% rate applies on the first €23 of taxable profits. We have recorded a valuation allowance equal to 100% of the value of our tax loss carry forwards. At the end of 2004, the Netherlands government enacted a tax rate reduction. As a result of this change in law, the Netherlands statutory tax rate will be reduced in steps to 30% through 2007.

Tax losses can be carried forward indefinitely and set off against future taxable profits. On January 1, 2001, a bill was enacted that may limit the ability to set off tax losses against future profits when the beneficial ownership of a company changes. This law could limit our ability to realize the benefits of our tax loss carry forwards in the future. We had tax loss carry forwards of €85,766, €68,802, and €55,289 at December 31, 2004, December 31, 2003 and December 31, 2002, respectively.

Research and Development

Our research and development spending totaled €20,468, €21,885 and €24,252 for the years 2004, 2003 and 2002, respectively. For a description of our research and development practices and policies, see "Item 4. Information on the Company—Research and Development."

Trend Information

Please see "Operating Results" and "Item 4. Information on the Company" for trend information.

Off-Balance Sheet Arrangements

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, changes in financial condition, revenues or expenses, results of operations, liquidity, capital expenditures or capital resources, that is material to investors.

Tabular Disclosure of Contractual Obligations and Commercial Commitments

Future minimum payments for all contractual obligations for years subsequent to December 31, 2004 are as follows:

	Total	Less than one year	1-3 years	3-5 years	More than 5 years
Contractual Obligations					
Operating leases	9,285	1,838	3,692	3,654	101
Capital leases, short term	1,345	1,345	—	—	—
Research and license	5,151	1,828	3,323	—	—
Other Long-Term Liabilities agreements					
Long term obligations capital leases	1,443	—	1,443	—	—
Long term obligations deferred revenues	4,198	—	4,198	—	—
Total	€21,422	€5,011	€12,656	€3,654	€101

As of December 31, 2004, certain lease agreements contain provisions whereby we are required to make immediate payment of all amounts due under the lease in the event our cash and cash equivalents balance falls below € 25,000 or stockholders' equity or cash and cash equivalents balance falls below € 75,000. As of December 31, 2004, €3,880 of amounts due under leases are subject to these provisions. As of March 2005 these covenants have been withdrawn for several contracts. Consequently only €1,800 of amounts due under leases is subject to these provisions as of March 2005.

Recent Accounting Pronouncements

In December 2004, the Financial Accounting Standards Board ("FASB") issued a revision of FASB statement No. 123, Accounting for Stock-Based Compensation ("SFAS No. 123 (R)"). This statement supersedes Accounting Principles Board ("APB") Opinion No. 25, Accounting for Stock Issued to Employees, and its related implementation guidance. SFAS No. 123 (R) addresses the accounting for share-based payment transactions in which a company receives employee services in exchange for either equity instruments of the company or liabilities that are based on the fair value of the company's equity instruments or that may be settled by the issuance of such equity instruments. SFAS No. 123 (R) eliminates the ability to account for share-based compensation transactions using the intrinsic method and generally requires that such transactions be accounted for using a "fair-value"-based method and recognized as expense in our consolidated statement of operations. SFAS No. 123 (R) is effective as of the beginning of the first interim or annual reporting period that begins after June 15, 2005. We are currently evaluating the impact of SFAS 123(R) on our consolidated financial statements.

Item 6. Directors, Senior Management and Employees

Directors, Senior Management and Board Practices

We have a two-tier board structure consisting of a management board (*raad van bestuur*), which manages our business, and a supervisory board (*raad van commissarissen*), which supervises and advises our management board.

At the annual general meeting of shareholders in 2004, our shareholders approved the amendment of our articles of association. Most of the amendments to the articles of association are based on the principles and provisions of the Dutch corporate governance code. For more information on our articles of association see Item 10—"Memorandum and Articles of Association."

Supervisory Board

Our supervisory board must approve certain resolutions of our management board, which are specified in our articles of association. In addition, our supervisory board may give our management board written notice of other corporate actions that it wishes to approve. In fulfilling their duties, all members of our supervisory board must serve our best interests.

Our articles of association provide that at least three supervisory board members must serve on our supervisory board. We must fill any vacancies on the supervisory board as soon as possible, but until they are filled the remaining members of our supervisory board constitute a competent board. Under Dutch law, supervisory board members cannot serve as members of our management board.

The members of our supervisory board are appointed for terms ending on the date of the first annual meeting of shareholders that is held four years after the date of their appointment. They may be reappointed for two consecutive terms of four years. The holder of our priority shares, Stichting Prioriteit Crucell, also referred to as the Priority Foundation, nominates the supervisory board members. There must be at least two nominees for each vacancy on the supervisory board. The general meeting can override these binding nominations by a vote of an absolute majority of the votes cast. This vote must represent more than one third of our issued share capital. If the holders of our priority shares do not make any nominations within three months after the vacancy has occurred, our general meeting of shareholders can fill supervisory board vacancies. If the holders of our priority shares made a non binding nomination, then an appointment in deviation with the nomination is only possible by a resolution of the general meeting of shareholders taken by an absolute majority of the votes cast, representing at least one third of our issued capital. The supervisory board members retire according to a rotation plan that the supervisory board establishes.

Our supervisory board appoints its own chairman and must adopt rules for its own internal governance and establish committees. The supervisory board must, in any event, establish an audit committee, a remuneration committee and a nomination committee. Passing supervisory board decisions requires a majority of the votes cast at a meeting of our supervisory board, unless otherwise provided for in the articles of association or the by-laws of the supervisory board. The supervisory board is assisted by a company secretary.

A supervisory board member can be suspended or dismissed at any time by a resolution of our general meeting of shareholders passed by an absolute majority of the votes cast. This vote must represent more than one third of our issued share capital. Within three months after a suspension, our general meeting of shareholders must either dismiss the supervisory director, terminate the suspension or extend it. The total suspension may not exceed three months.

The general meeting of shareholders determines the supervisory board members' compensation. In contrast to the provisions of the Dutch corporate governance code, we pay our supervisory board

members in options on our ordinary shares as well as cash, and reimburse them for their expenses. See "Remuneration of the Management Board and Supervisory Board."

The business address of each supervisory board member is the address of our principal executive office in Leiden, The Netherlands. As of March 31, 2005 our supervisory board members held an aggregate of 269,188 of our ordinary shares. See "Share Ownership."

The following table sets forth the name, age and position of each of the members of our supervisory board:

Name	Age	Position	Service period according to rotation scheme
Pieter Strijkert	69	Chairman	2006
Jan Oosterveld	61	Member	2007
Phillip Satow	63	Member	2006
Claes Wilhelmsson	66	Member	2005
Seán Lance	57	Member	2005

Mr. Deleage and Mr. Van Beneden resigned from the supervisory board on June 3, 2004 when their terms expired.

Mr. Arnold Hoevenaars is expected to be nominated by the Priority Foundation to be appointed to the supervisory board by the annual meeting of shareholders scheduled for June 2005. In anticipation of his nomination, Mr. Hoevenaars has attended supervisory board meetings as an observer since July 2004.

Mr. Domenico Valerio was appointed a member of our supervisory board, effective January 1, 2005, at our annual meeting of shareholders in June 2004. In January 2005, Mr. Valerio and we agreed that he would not serve as a member of our supervisory board, but would continue to serve us in an advisory role with an emphasis on investor and public relations.

The following paragraphs contain brief biographies of each of our supervisory board members:

Pieter Strijkert has served as chairman of our supervisory board since our incorporation. He also served as chairman of the supervisory board of IntroGene from 1994 to October 2000, and as chairman of the supervisory board of U-BiSys from 1998 to October 2000. He currently serves on the boards of Chiron Corporation, a position he has held since 1987, and Paratek Pharmaceuticals, Inc., a position he has held since 1998. He served as chairman of the supervisory boards of Pharming from 1995 to 2001, and for deVGen N.V. and PamGene B.V. from 2000 to 2003. From 1985 to 1995 he was a member of the managing board of Gist-Brocades N.V. Mr. Strijkert has a PhD from the University of Utrecht.

Jan Oosterveld retired from Royal Philips Electronics N.V. on April 1, 2004, after an international career of 32 years. He was responsible for Corporate Strategy, Corporate Alliances and the joint ventures with LGE on CRT and LCD. In the latter responsibility he was the Chairman of the Board of LG.Philips Ltd, which went public in April 2004 and Vice-Chairman of the Board of LG.Philips Displays BV. He was also the CEO of Philips Asia Pacific. He graduated as a Mechanical Engineer 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. Mr. Oosterveld has served as a member of our supervisory board since May 2004. He is appointed as member during the annual general meeting of shareholders on June 3, 2004. He is also a member of the Board of Barco, Kortrijk, Belgium, Atos Origin, Paris, France, Cookson Electronics Group, London, UK and Continental, Hannover, Germany.

Phillip Satow has served as a member of our supervisory board since our incorporation. He spent 14 years at Pfizer, Inc. where his last position was vice president, Pfizer Europe. From 1985 to 1997, he

was executive vice president of marketing at Forest Laboratories, Inc. From 1998 to 1999 he was president of Forest Pharmaceuticals, executive vice president of Forest Laboratories Inc. and a member of its board of directors. Mr. Satow currently serves on the public boards of Forest Laboratories Inc. (FRX), and Eyetech Pharmaceuticals Inc. (EYET) and is Chairman and CEO of JDS Pharmaceuticals LLC, a privately held pharmaceutical company. Mr. Satow received a Masters in Economics from Georgetown University.

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, where he was 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 Astra, he was a lecturer and researcher at the University of Göteborg in Sweden, where he also completed his medical education and PhD. He currently serves on the boards of a number of biotechnology and start-up companies. Dr. Wilhelmsson previously served on the board of AstraZeneca PLC.

Seán Lance has served as a member of our supervisory board since January 2004. Mr. Lance is the past chairman of Chiron Corporation. He joined Chiron as president and chief executive officer in 1998. From 1985 to 1998 he was employed at Glaxo Holdings where his last position was group chief operating officer and CEO designate. He is a past president of the International Federation of Pharmaceutical Manufacturers Association. Mr. Lance is a chartered company secretary and administrator and he also holds a post-graduate qualification in Advanced Financial Management.

Arnold Hoevenaars has been attending our supervisory board meetings as an observer since July 2004. We expect that he will be nominated by the Priority Foundation as an independent supervisory board member, and that shareholder approval for his appointment shall occur at our next Annual General Meeting, scheduled for 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 Chief Financial Officer of Royal Boskalis Westminster N.V.

Remuneration Committee

Our supervisory board has established a remuneration committee. The remuneration committee determines our policy on remuneration of all members of our management board and management committee. See "Remuneration of the Management Board and Supervisory Board—Remuneration Policy". The members of our remuneration committee are Phillip Satow (Chairman), Pieter Strijkert and Claes Wilhelmsson.

Audit Committee

Our supervisory board has established an audit committee. The audit committee consists of three supervisory board members who are independent within the meaning of the Nasdaq listing rules. This committee has responsibility for, among other things, reviewing our annual and interim reports and accounts and monitoring our auditors' involvement in that process. The ultimate responsibility for reviewing our annual and interim accounts lies with our supervisory board. The members of our audit committee are Seán Lance (Acting Chairman), Jan Oosterveld and Pieter Strijkert. Arnold Hoevenaars has attended audit committee meetings as an observer since July 2004.

Nomination Committee

Our supervisory board has established a nomination committee, which is expected to take over the nomination responsibilities of the Priority Foundation. The nomination committee consists of all supervisory board members. This committee (a) draws up selection criteria and appointment

procedures for members of the supervisory board and the management board, (b) periodically assesses the size and composition of the supervisory board and the management board and makes a proposal for a composition profile of the supervisory board, (c) periodically assesses the functioning of individual members of the supervisory board and the management board, and reports on this to the supervisory board and (d) supervises the policy of the management board on the selection criteria and appointment procedures for senior management. The committee also makes proposals for appointments of management board members to the supervisory board and for appointments of supervisory board members to the holders of priority shares.

Scientific Committee

Our supervisory board has established a scientific committee. The scientific committee consists of one supervisory board member who is independent within the meaning of the Nasdaq listing rules. This committee has responsibility for, among other things, reviewing progress in our research and development activities. The chairman and sole member of our scientific committee is Claes Wilhelmsson.

Management Board

Our management board manages our general affairs and business, under the supervision of our supervisory board. Under our articles of association, the management board requires prior approval of the supervisory board for resolutions to:

- expand into a new, or cease an existing, line of business;
- participate in, sell an interest in, or change its participation in, or otherwise take an interest in, or assume the management of another business enterprise;
- enter into, terminate or amend any joint venture or pooling arrangement;
- acquire fixed assets exceeding price limits set by the supervisory board; and
- enter into financial commitments exceeding price limits set by the supervisory board or for longer than a year.

Under Dutch law, in certain circumstances, management board actions may require the approval of the general meeting of shareholders.

Our supervisory board determines the size of our management board after consultation with our chief executive officer. Our general meeting of shareholders appoints the members of our management board from binding nominations made by our supervisory board. There must be at least two nominees for each vacancy on our management board. The general meeting of shareholders can override these binding nominations by a vote of an absolute majority of the votes cast. This vote must represent more than one third of our issued share capital. If our supervisory board does not nominate anyone for a specific position within three months after the vacancy has occurred, our general meeting of shareholders can appoint a replacement by an absolute majority of votes. If the supervisory board makes a non binding nomination, then an appointment contrary to the nomination is only possible by a resolution of the general meeting of shareholders taken by an absolute majority of the votes cast, representing at least one third of our issued capital.

Our management board may establish rules governing its internal organization. Our supervisory board must approve the adoption of and any changes to these rules. Our management board may charge each member of the management board with particular duties. The allocation of duties requires the approval of the supervisory board. Resolutions of our management board require a majority of votes cast, unless provided otherwise in the by-laws of the management board. The management board

may appoint a company secretary who will assist the management board. The appointment and removal of the company secretary requires the prior approval of the supervisory board.

A management board member can be suspended or dismissed and a suspension can be lifted by a resolution of an absolute majority of the votes cast at a shareholders meeting. This vote must represent more than one third of the issued share capital. Our supervisory board may also suspend (but not dismiss) a member of our management board. We must hold a general meeting of shareholders within three months after a suspension to either terminate or extend it. The total suspension may not exceed three months.

Our supervisory board determines the compensation and benefits of the members of our management board, on a proposal by the remuneration committee, within the scope of the remuneration policy adopted by the general meeting of shareholders. The business address of the members of our management board is the same as the address of our principal executive office in Leiden, The Netherlands.

The name, age and position of the members of our management board are:

Name	Age	Position
Ronald H.P. Brus	41	Chairman of the management board, president and chief executive officer
Jaap Goudsmit	53	Chief scientific officer
Leonard Kruimer	46	Chief financial officer

On January 26, 2004, Domenico Valerio stepped down as president, chief executive officer and chairman of our management board. Ronald H.P. Brus, formerly our chief operating officer was appointed as Mr. Valerio's successor in these positions. In addition, Jaap Goudsmit, our chief scientific officer, was appointed as member of the management board. Mr. Valerio was appointed a member of our supervisory board, effective January 1, 2005, at our annual meeting of shareholders in June 2004. In January 2005, we and Mr. Valerio agreed that he would not serve the Company as a member of our supervisory board, but would continue to serve us in an advisory role with an emphasis on investor and public relations. Leonard Kruimer, our chief financial officer, joined the management board as of January 1, 2005.

We are currently in the process of entering into new employment contracts with each member of our management board, and we expect that these contracts will be effective by June 2005. The fixed remuneration of our chief executive officer, Ronald H.P. Brus, is not reflected in his current employment contract, but rather has been set by resolution of our remuneration committee. See "—Remuneration of the Management Board and Supervisory Board." Our chief scientific officer, Jaap Goudsmit, voluntarily elected to receive fixed remuneration in 2004 lower than he is entitled to pursuant to the terms of his current employment contract, based on his reflection on the current biotech industry climate at the time.

The employment contracts of Mr. Brus, Mr. Goudsmit and Mr. Kruimer contain non-compete provisions that would apply for a period of one year after the end of their employment with us.

Management committee

We have a management committee. The management board determines the number of members of the management committee. Members of the management committee are appointed and dismissed by the management board, with the approval of our supervisory board. The management committee advises the management board in strategic, general managerial and executive matters and assists the management board in implementing these matters. The management committee generally meets twice a month, and works closely with other members of our management team. Our management board may

establish rules governing its relationship with our management committee. Our supervisory board must approve the adoption of and any changes to these rules.

The following table sets forth the name, age and position of each of the members of our management committee:

Name	Age	Position
Ronald H.P. Brus	41	Chairman of management board, president and chief executive officer
Jaap Goudsmit	53	Chief scientific officer
Leonard Kruimer	46	Chief financial officer
René K. Beukema(1)	41	General counsel and corporate secretary
Jean-Yves Guichoux(1)	58	Executive vice-president development
Arthur Lahr(1)	36	Vice-president business development

(1)

René K. Beukema, Jean-Yves Guichoux and Arthur Lahr became members of our management committee as of January 31, 2004.

The following paragraphs contain brief biographies of the members of our management board and the members of our management committee:

Ronald H.P. Brus is chairman of the management board and president and chief executive officer since January 26, 2004, and has been a member of our management committee since our incorporation. He was executive vice president, business development at IntroGene from 1997 to 2000 and chief operating officer at Crucell from March 2003 through to his appointment as president and chief executive officer. From 1994 to 1996, he was product-planning physician at Forest Laboratories (New York) and from 1990 to 1994 he was medical director for Zambon B.V. He holds a medical degree (M.D.) from the University of Groningen.

Jaap Goudsmit is a member of the management board since January 26, 2004. He was our Senior Vice President Vaccine Research from September 2001 until July 2002 and member of our management committee from July 2002 as Executive Vice President Vaccine R&D. In September 2002 he was appointed Chief Scientific Officer and head of Research and Development. He chaired at the Academic Medical Center of the University of Amsterdam the Research Institute for Infectious Diseases and the Institute for Science Education. He was the founding chair of the Scientific Advisory Committee of the International AIDS Vaccine Initiative (IAVI) and the founding co-chair of the European Vaccine Effort against HIV/AIDS (EuroVac). Since 1989 he has been a professor at the University of Amsterdam and the Academic Medical Center. He holds a medical degree (MD) and a PhD from the University of Amsterdam and is a board certified medical microbiologist.

Leonard Kruimer became a member of the management board on January 1, 2005. He has been our chief financial officer and a member of our management committee since our 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. He holds a Masters in Business Administration from Harvard Graduate School of Business Administration, a degree from the University of Massachusetts, Amherst, and is a CPA in New York State.

René K. Beukema has been our general counsel and corporate secretary since our incorporation. He held the same position at IntroGene from 1999 to 2000. From 1994 to 1999 Mr. Beukema was Senior Legal Counsel for GE Capital/TIP Europe. From 1991 to 1994, he was legal counsel for TNT Express Worldwide N.V. He has a Masters in Law from the University of Amsterdam.

Jean-Yves Guichoux has been our executive vice president of development since December 2003. He most recently served as vice president at Afforce Healthcare. Prior to joining Afforce, he worked at Yamanouchi Europe in The Netherlands, where he headed the clinical research department. Mr. Guichoux also spent over 10 years at the European research headquarters of Wyeth-Ayerst, where he held the position of vice president, clinical research and development. In this function, he directed the company's Phase I through IV product development programs across multiple therapeutic areas. Previously, Mr. Guichoux spent 11 years as director of the medical department for Wyeth's French affiliate. He also worked as medical director for Lafon and as medical advisor for Lepetit. Mr. Guichoux received his medical degree (M.D.) from the University of Rennes in France in 1971.

Arthur Lahr was appointed vice president of business development in December 2003 and a member of the management committee in January 2004. He joined Crucell in April 2001 as executive director, business development. From 1994 to 2001 he was a consultant at McKinsey & Co. in The Netherlands and New York. Prior to that he worked with Unilever. He holds a Masters in Business Administration from INSEAD and a Masters in Science, Applied Physics, from the University of Delft.

Management Committee Service Contracts

The service contract with Jaap Goudsmit provides for benefits upon termination of employment in deviation with the provisions of the Dutch corporate governance code. In addition, the supervisory board approved in May 2003 a proposal to permit severance payments to members of the management committee and certain other senior executives in case of a change of control. In the event a change of control of the Company occurs, the following management committee members would receive severance payments equal to their salaries in the number of months indicated: Ronald H.P. Brus (24 months), Jaap Goudsmit (21 months), Leonard Kruimer (21 months) and René Beukema (18 months).

Disclosure Committee

In March 2003, we established a disclosure committee designed to help senior management, particularly the chief executive officer and chief financial officer, in the maintenance and evaluation of our disclosure controls and procedures. The disclosure committee gathers all relevant financial and non-financial information and assesses materiality, timeliness and necessity for disclosure of such information. The disclosure committee is comprised of the members of the management committee and the management team. The management team members are the director of finance and planning, vice president of intellectual property and licensing, director for quality affairs, executive director vaccine research, director antibody research, director investor relations and communications, director human resources and manager facilities. Members of the disclosure committee have direct access to our external legal counsel and our external auditor. The disclosure committee reports to the chief executive officer and chief financial officer. The chief executive officer and chief financial officer have also re-emphasized the importance of internal controls at our Company in an effort to facilitate continuous improvement of internal control procedures and reporting.

We believe that the establishment of the disclosure committee and additional actions taken for further improvement of disclosure and internal controls comply with the requirements of the Sarbanes-Oxley Act of 2002 and recent regulations promulgated by the Securities and Exchange Commission under that Act.

Remuneration of the Management Board and Supervisory Board

Netherlands legislation requires full disclosure of individual management board and supervisory board remuneration. We have included the required disclosures below.

Remuneration Policy

The remuneration committee is charged by the supervisory board to review and recommend specific compensation and benefit levels for the members of the management board and the members of the management committee in consultation with the management board. In addition, the remuneration committee reviews the general compensation and benefit policies for our employees.

The remuneration committee advises on policies and reviews and determines objectives relevant to the compensation of the members of the management board and members of the management committee. Remuneration consists of a fixed salary portion and a variable bonus portion that is linked to our overall performance and the achievement of set objectives. The remuneration committee evaluates the performance of members of the management board and management committee in view of those objectives and advises on the fixed and variable compensation of members of the management board and the management committee. In advising on short and long term incentive compensation for members of the management board and management committee, the remuneration committee considers among other factors our financial and commercial performance, scientific performance and progress, and the accrual of value of the Company. External compensation survey data available for the biotechnology industry are also used as another factor to benchmark the compensation levels. It is the aim of the remuneration committee to position the remuneration packages for members of the management board and management committee at competitive levels. The bonus paid to the management board is paid in connection with achievement of certain objectives set by the supervisory board.

Our remuneration policy is currently being reviewed by an external compensation and benefits consultancy firm, and we expect that the policy will be submitted to the general meeting of shareholders in 2005.

Management Board

The total remuneration and related costs of the members of the management board over the past three years, excluding stock options, is as follows:

	Year ended December 31,		
	2004	2003	2002
Salaries	€ 598	€ 356	€ 619
Bonuses	494	—	94
Pension costs(1)	215	91	146
Severance costs	454(3)	—	650(2)
Totals	€ 1,761	€ 447	€ 1,509

(1) Pension costs include disability insurance costs of 19.3% of the total amount.

(2) Upon the termination of his employment contract and resignation from our management board on September 9, 2002, Ton Logtenberg received a one-time severance payment of €650. On that date, we entered into a consulting agreement with him whereby he receives compensation of €5 per month. The consulting agreement is scheduled to end January 19, 2006.

(3) In connection with his stepping down as our chief executive officer, president and chairman of our management board, we agreed to pay Mr. Valerio an amount equal to €454 in severance and up to €19 as partial compensation for advisory costs. On January 26, 2004, we also entered into an advisory agreement with Mr. Valerio under which he received an advisory fee totaling €227 through the end of 2004.

The remuneration of the individual members of our management board during 2004, excluding stock options, was as follows:

	<u>Base salary</u>	<u>Bonus</u>	<u>Other Benefits(1)</u>	<u>Total</u>
Ronald H.P. Brus	€ 289	€ 296	€ 76	€ 661
Jaap Goudsmit	€ 281	€ 193	€ 196	€ 670
Domenico Valerio(2)	€ 28	€ 5	€ 98	€ 132
Totals	€ 598	€ 494	€ 370	€ 1,463

(1) "Other benefits" include company cars, social security costs and disability insurance.

(2) Domenico Valerio stepped down from our management board on January 26, 2004.

For details regarding share and option ownership by our management board members, see "Share and Option Ownership."

Pension, retirement and similar arrangements for our management board members consist of a defined contribution plan, and we do not have further pension obligations beyond the annual premium contribution.

The total remuneration and related costs of our management committee in 2004, excluding those of the management board members, was €1,517, excluding stock options.

Supervisory Board

During 2004, the individual members of the supervisory board received the following remuneration, excluding stock options. The remuneration was based on a fixed amount of €5 per member, an additional payment of €5 for each chairmanship of a committee, and payments based on the actual number of supervisory board meetings attended, as well as an additional payment of €4.9 to cover expenses for the chairman. We reimburse our supervisory board members for their travel and associated expenses incurred in connection with supervisory board meetings. The remuneration for the members of the supervisory board is determined by the general meeting of shareholders.

	<u>2004</u>	<u>2003</u>
Pieter Strijkert	24.9	27.5
Michiel de Haan	N/A	25.0
Jan Oosterveld	22.5	N/A
Phillip Satow	20.0	22.5
Claes Wilhelmsson	20.0	25.0
Seán Lance	22.5	N/A
Jean Deleage	5.0	17.5
Patrick van Beneden	5.0	22.5
Totals	119.9	140.0

For details regarding share and option ownership by our supervisory board members, see "Share and Option Ownership."

Share and Option Ownership

As of December 31, 2003, December 31, 2004 and March 31, 2005, members of our management board and supervisory board held the following options and as of March 31, 2005, the following ordinary shares. Options generally expire in December or January of the relevant year.

Name of holder	Numbers of ordinary shares held per March 31, 2005	% of total ordinary shares	Options held per December 31, 2003	Year of expiration	Exercise price(s)	Granted 2004(1)	Exercised 2004	Forfeited 2004	Options held per December 31, 2004	Options held per March 31, 2005
Management board:										
Ronald H.P. Brus	79,697	0.21	56,250	2005	11.43	—	—	—	56,250	—
			75,000	2005	7.35	—	—	—	75,000	75,000
			225,000	2011	3.49	—	—	—	225,000	225,000
			90,000	2011	2.64	—	—	—	90,000	90,000
			125,000	2011	5.94	—	—	—	125,000	125,000
			—	2009	9.40	250,000	—	—	250,000	250,000
Jaap Goudsmit	—	—	100,000	2005	7.96	—	—	—	100,000	100,000
			100,000	2006	5.92	—	—	—	100,000	100,000
			100,000	2006	3.66	—	—	—	100,000	100,000
			60,000	2011	2.64	—	—	—	60,000	60,000
			125,000	2011	5.94	—	—	—	125,000	125,000
			—	2009	9.40	85,000	—	—	85,000	85,000
Leon Kruimer	12,700	0.03	26,250	2005	11.43	—	—	—	26,250	—
			105,000	2011	3.49	—	—	—	105,000	105,000
			125,000	2011	5.94	—	—	—	125,000	125,000
			—	2009	9.40	85,000	—	—	85,000	85,000
Domenico Valerio	N/A	N/A	502,500	2011	3.49	—	—	—	502,500	N/A
			125,625	2005	11.43	—	—	—	125,625	—
Subtotal	92,397	0.24	1,940,625			420,000	0	0	2,360,625	1,650,000
Supervisory board:										
Pieter Strijkert	195,188	0.52	79,474	2005	0.49	—	—	—	79,474	—
			4,500	2005	11.43	—	—	—	4,500	—
			8,000	2005	7.16	—	—	—	8,000	8,000
			24,000	2011	3.49	—	—	—	24,000	24,000
			10,000	2011	6.48	—	—	—	10,000	10,000
			—	2009	11.55	10,000	—	—	10,000	10,000
Jan Oosterveld	—	—	—	2009	8.81	10,000	—	—	10,000	10,000
			—	2009	11.55	10,000	—	—	10,000	10,000
Phillip Satow	74,000	0.20	3,000	2005	11.43	—	—	—	3,000	—
			7,000	2005	7.16	—	—	—	7,000	7,000
			22,000	2011	3.49	—	—	—	22,000	22,000
			10,000	2011	6.48	—	—	—	10,000	10,000
			—	2009	11.55	10,000	—	—	10,000	10,000
Claes Wilhelmsson	—	—	10,000	2011	6.48	—	—	—	10,000	10,000
			—	2009	11.55	10,000	—	—	10,000	10,000
Seán Lance	—	—	—	2011	7.86	10,000	—	—	10,000	10,000
			—	2009	11.55	10,000	—	—	10,000	10,000
Patrick van Beneden(2)	N/A	N/A	7,000	2005	7.16	—	—	—	7,000	N/A
Jean Deleage(2)	—	—	3,000	2005	11.43	—	—	—	3,000	N/A
			7,000	2005	7.16	—	—	—	7,000	—
			10,000	2007	6.49	—	—	—	10,000	—
			22,000	2011	3.49	—	—	—	22,000	—
Subtotal	269,188	0.72	226,974			70,000	0	0	296,974	161,000
Total	361,585	0.96	2,167,599			495,000	0	0	2,657,599	1,811,000

(1) In April 2004, the supervisory board approved a new option plan whereby employees and supervisory board were granted options with an exercise price 126% greater than the average closing stock price of the Company on the three days preceding the option grant date and have a five year life.

(2) Mr. Deleage and Mr. Van Beneden resigned from the supervisory board on June 3, 2004 when their term expired.

We account for stock-based compensation under the fair value method in accordance with the provisions of Financial Accounting Standards Board Statement No. 123 (SFAS 123), Accounting for Stock-Based Compensation. Under SFAS 123, the fair market value of a stock option is determined at the time of grant and recorded on our balance sheet as deferred compensation, which we then amortize over the vesting period. At December 31, 2004, we had €4,958 of deferred compensation. See note 6 to our financial statements included elsewhere in this annual report.

In April 2004, the supervisory board approved a new option plan whereby employees and supervisory board are granted options with an exercise price 126% greater than the average closing stock price of the Company on the three days preceding the option grant date and have a five year life. The options are subject to profit retribution provisions. Such provisions entitle us for a period of three years from issuance to receive a portion of any profits upon the sale of the shares, calculated as the difference between the total proceeds from the sale of shares, and the aggregate selling price. The portion of the profits payable to the Company decreases ratably over three years. The relevant portion of any profits derived by the employee from the sale of shares received on exercise of options must be remitted to us if the employee terminates employment prior to the end of the three year period. A total of 963,500 options with an exercise price of €9.40 per share were granted under the new option plan, resulting in deferred compensation of €3,141. Compensation expense is recognized ratably over a period of three years; €1,047 or €1.09 per option per twelve months. As of September 2004, under Dutch law, stock options and share plans need the prior approval of the general meeting of shareholders.

As of March 31, 2005, there were 1,273,984 options (or approximately 2% of our issued share capital) available to be granted to our employees and to our supervisory board members.

Corporate Governance Developments

We continuously monitor and assess applicable corporate governance rules, including recommendations and initiatives regarding principles of corporate governance. These include those that have been developed in the United States both by the NASDAQ National Market ("Nasdaq") and by the SEC pursuant to the Sarbanes-Oxley Act of 2002, some of which already are applicable and some of which will be applicable to the Company during 2006. On March 10, 2003, the Netherlands government commissioned a committee known as the Tabaksblat Committee to conduct a review of corporate governance in the Netherlands. The Tabaksblat Committee issued its final report "The Netherlands Corporate Governance Code" (the "Code") on December 9, 2003, which came into effect as of the financial year starting on or after January 1, 2004. On September 1, 2004, new provisions were added to Section 2:391 of the Dutch Civil Code, giving the possibility to add by governmental decree requirements on the contents of annual reports. These requirements specifically relate to the compliance with a code of conduct designated as such by the governmental decree. On December 23, 2004, such governmental decree was issued for Dutch listed companies, providing that the Code was designated as code of conduct and that a public company should include in its annual report a statement about the compliance with the principles and best practice provisions of the Code that are aimed at the management board or supervisory board. The governmental decree requires that a company states in its annual report if it did not comply with the principles or best practice provisions of the Code, or if it does not have the intention to do so during the current or following financial year. The governmental decree applies to the annual report that relates to the financial year starting on or after January 1, 2004. A report on compliance with the Code is required to be included in the Dutch statutory annual report for the financial year 2004. The Code contains recommendations with regard to corporate governance, including the following topics:

- strengthening the role of the supervisory board and its committees and to increase its independence, quality and expertise;

- strengthening the role of the shareholders with respect to control on the functioning of the management board and the supervisory board, as well as with respect to nomination and remuneration of members of the management board and the supervisory board;
- facilitating and stimulating shareholders to use their voting power and to actively participate in the general meeting of shareholders;
- 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.

We are currently implementing applicable provisions of the Code and the Sarbanes–Oxley Act of 2002, and subsequent SEC and Nasdaq rules that have been issued pursuant thereto.

Exemptions from Certain Nasdaq Corporate Governance Rules

Nasdaq rules provide that Nasdaq may provide exemptions from the Nasdaq corporate governance standards to a foreign issuer when those standards are contrary to a law, rule or regulation of any public authority exercising jurisdiction over such issuer or contrary to generally accepted business practices in the issuer's country of domicile. We have received from Nasdaq exemptions from certain Nasdaq corporate governance standards that are contrary to the laws, rules, regulations or generally accepted business practices of The Netherlands. These exemptions and the practices followed by our company are described below:

- We are exempt from Nasdaq's quorum requirements applicable to meetings of shareholders. In keeping with Netherlands law and Netherlands generally accepted business practice, our articles of association provide that there are no quorum requirements generally applicable to general meetings of shareholders.
- We are exempt from Nasdaq's requirements regarding the solicitation of proxies and provision of proxy statements for meetings of shareholders. We inform shareholders of meetings in a public notice, but we do not solicit proxies for general meetings of shareholders. Netherlands law does not have a regulatory regime for the solicitation of proxies and the solicitation of proxies is not a generally accepted business practice in The Netherlands. In connection with our American Depositary Shares ("ADSs"), the Bank of New York, as depositary under our depositary agreement relating to our ADSs, distributes proxy materials to holders of our ADSs.
- We are exempt from Nasdaq's requirements regarding shareholder approval. In keeping with Netherlands law and Netherlands generally accepted business practices, our articles of association do not include a shareholder approval requirement. Our articles of association provide that the general meeting of shareholders may resolve to amend our articles of association, or dissolve, merge or demerge the Company, if our supervisory board first proposes the measure.
- We do not distribute annual reports to all of our shareholders in accordance with Nasdaq rules. As our shares are bearer shares according to Netherlands law, we are not able to distribute to shareholders copies of annual and interim reports. Copies of such reports are available to shareholders at our corporate headquarters, and are filed with Nasdaq and the Bank of New York as depositary under our depositary agreement relating to our ADSs. Under the terms of the depositary agreement, the Bank of New York distributes our annual reports to holders of our ADSs.

Limitation of Liability and Indemnification Matters

Pursuant to Dutch law, each member of our supervisory and management boards is responsible to the Company for the proper performance of his or her assigned duties. They are also responsible for taking measures to prevent the consequences of any improper performance of duties by another member of our supervisory or management board. Our articles of association provide that our supervisory and management board members are discharged from liability for their actions as board members, if our general meeting of shareholders adopts a resolution to that effect. This discharge extends only to actions or omissions disclosed in or apparent from the adopted annual accounts or otherwise communicated to our general meeting of shareholders.

This discharge of liability may be limited by mandatory provisions of Dutch law, such as in the case of bankruptcy. Under Dutch law, our supervisory board members and the members of our management board generally cannot be held personally liable for decisions made exercising their reasonable business judgment.

Our articles of association provide that we shall generally indemnify any person who is or was a member of our supervisory board or our management board or one of our employees, officers or agents, and suffers any loss as a result of any action in connection with their service to us, provided they acted in good faith in carrying out their duties.

This indemnification generally will not be available if the person seeking indemnification acted with gross negligence or willful misconduct in the performance of their duties to the Company. A court in which an action is brought may, however, determine that indemnification is appropriate nonetheless.

Employees

As of December 31, 2004, we had 210 full-time equivalents direct and indirect employees of whom 171 were engaged in, or directly support, research and development activities and 39 were employed in administrative and business development positions.

As of December 31, 2003, we had 182 full-time equivalents direct and indirect employees of whom 151 were engaged in, or directly support, research and development activities and 31 were employed in administrative and business development positions.

As of December 31, 2002, we had 183 full-time equivalents direct and indirect employees of whom 154 were engaged in, or directly support, research and development activities and 29 were employed in administrative and business development positions.

In 2003, we established a workers council for our employees in compliance with certain Dutch legal requirements. The workers council is a representative body that consists of seven elected employees. The management board is required to seek the non-binding advice of the workers council before making certain major decisions, such as those relating to a major acquisition, a change of control or the appointment or dismissal of a management board member. The workers council must also be consulted in connection with any material change affecting all employees or certain groups of employees, including with respect to any changes to our employee benefits programs. No collective bargaining agreements are applicable to our employees. We believe that our relations with our employees are generally good.

Item 7. Major Shareholders and Related Party Transactions

Major Shareholders

The following table sets forth certain information concerning the beneficial ownership of our ordinary shares as of March 31, 2005 by:

- each shareholder who is known by us to beneficially own 5% or more of our outstanding ordinary shares; and
- our supervisory board members and management board members, each as a group.

Percentage of beneficial ownership is based on an aggregate of 37,352,254 ordinary shares outstanding at March 31, 2005.

Beneficial Owner	Ordinary Shares Beneficially Owned(1)	
	Number of Ordinary Shares	Holding (%)
Aviva plc./Delta Lloyd Levensverzekeringen N.V.	—	5.02(2)
A. van Herk B.V	—	5.15(3)
Ordinary shares held by the members of our management board as a group	92,397	0.24
Ordinary shares held by our supervisory board members as a group	269,188	0.72

- (1) Under Rule 13d-3 of the Exchange Act, more than one person may be deemed to beneficially own certain ordinary shares (if, for example, persons share the power to vote or the power to dispose of the ordinary shares). In addition, a person is deemed to beneficially own ordinary shares if the person has the right to acquire the ordinary shares (for example, upon exercise of an option) within 60 days of the date as of which the information is provided. As a result, the percentage of outstanding ordinary shares of any person as shown in this table does not necessarily reflect the person's actual ownership or voting power with respect to the number of ordinary shares actually outstanding. These numbers include options held by shareholders because options are exercisable on grant. In addition, filings with The Netherlands Authority for the Financial Markets (*Autoriteit Financiële Markten*) with respect to shareholdings in public companies do not specify the number of shares held by the filing party.
- (2) Percentage holding is derived from a filing made by Aviva plc. /Delta Lloyd Levensverzekeringen N.V. with The Netherlands Authority for the Financial Markets (*Autoriteit Financiële Markten*) on February 1, 2005. The number of shares held was not filed.
- (3) Percentage holding is derived from a filing made by A. van Herk with The Netherlands Authority for the Financial Markets (*Autoriteit Financiële Markten*) on January 26, 2005. The number of shares held was not filed.

As of March 31, 2005 there were 11,881,164 ADSs, each representing one ordinary share, all of which were held of record by nine registered holders in the United States (including The Depository Trust Company). The number of ADSs at March 31, 2005 represent 31.8% of our ordinary shares that were issued and outstanding on that date.

To the best of our knowledge, we are not directly or indirectly controlled by any other corporation, foreign government or other entity.

Obligations of Shareholders to Disclose Holdings under Netherlands Law

The Netherlands' Act on Disclosure of Holdings in Listed Companies (the "Major Holdings Act") applies to any person or entity that, directly or indirectly, acquires or disposes of an interest in the voting rights and/or the capital of a public limited company incorporated under the laws of The Netherlands that is officially listed on a stock exchange within the European Union (the "EU"). Disclosure is required when, as a result of an acquisition or disposal, the percentage of voting rights or capital interest acquired or disposed of by a person or an entity reaches, exceeds or falls below 5, 10, 25, 50 or 66 ²/₃ percent. With respect to us, the Major Holdings Act would require any person or entity whose interest in our voting rights and/or capital reached, exceeded or fell below those percentage interests to notify in writing both us and The Netherlands Authority for the Financial Markets (*Autoriteit Financiële Markten* or *AFM*) immediately after the acquisition or disposal of the triggering interest in our share capital. Upon receipt of the notification, the AFM will disclose the information, as notified, to the public by means of an advertisement in a newspaper distributed throughout The Netherlands.

In addition, the members of our management and supervisory boards are required to immediately notify the AFM of any change in our 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. Noncompliance with the obligations of the Major Holdings Act can lead to criminal prosecution. In addition, a civil court can issue orders against any person who fails to notify or incorrectly notifies in accordance with the Major Holdings Act, including suspension of the voting rights in respect of such person's ordinary shares.

Related Party Transactions

Transactions Involving Our Senior Management

The following table describes all loans made to members of our management board and senior management since January 1, 2001. We have not made any loans to any of our supervisory board members. The interest rate on all loans was 4.5% per annum in 2002, 4.4% per annum in 2003, and 3.5% per annum in 2004. We set these interest rates in relation to Dutch income tax law, which changes on an annual basis. These loans become payable at the time shares received on exercise of related options are sold or, if the employee ceases to work for us before this time, immediately. We extended these loans prior to July 30, 2002, the date legislation was passed in the United States, prohibiting the grant of additional loans to company officers, and no loans or our senior management have been extended since that date. The loans to the persons listed below were extended in connection with options granted to them on our ordinary shares, and related taxes.

Name	Largest amount of loan outstanding since January 1, 2001	Amount of loan outstanding at March 31, 2005	Current Interest Rate
Ronald H.P. Brus	€ 132	€ 132	3.5%
Jaap Goudsmit	€ 25	€ 25	3.5%
René K. Beukema	€ 59	€ 54	3.5%

Loans to Ronald H.P. Brus for an amount of €13 provide that he will not owe us interest with respect to the entire principal of these loans. In each case, we cancel a certain portion of the interest owed to us and the associated income tax, and attribute such cancelled amounts to salary for income tax purposes.

Neither we nor any of our subsidiaries was a party to any material transactions, or proposed transactions, in which any director, any executive officer, any spouse or relative of any of the foregoing, or any relative of any such spouse had or was to have a direct or indirect material interest.

Item 8. Financial Information

See Item 18, "Financial Statements."

Legal Proceedings

In the ordinary course of business, we have been involved in certain disputes. Neither we, nor any of our subsidiaries, has been party to any legal or arbitration proceedings that may have, or have had during the 12 months preceding the date of this document, a significant effect on our financial position or any of our subsidiaries nor, as far as we are aware, are any such legal proceedings pending or threatened.

Dividends and Dividend Policy

Neither we nor our principal subsidiaries, Crucell Holland B.V., U-BiSys B.V. and ChromaGenics B.V., have ever declared or paid dividends. We do not intend to pay dividends on our ordinary shares for the foreseeable future. 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 U.S. dollars in respect of dividends on the underlying ordinary shares in accordance with a deposit agreement dated October 26, 2000, between The Bank of New York and us.

Significant Changes

Other than as disclosed in this annual report, no significant change has occurred since December 31, 2004, the date of our most recent audited financial statements.

Item 9. The Offer and Listing

Our ordinary shares are traded in the United States 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 acting as Depositary in respect thereof.

As of March 31, 2005, 37,352,254 ordinary shares were issued and outstanding. On the same date, there were 11,881,164 ADSs, each representing one ordinary share.

Our ordinary shares have been listed on the Official Market of Euronext Amsterdam N.V. (formerly Amsterdam Exchanges N.V.) since October 25, 2000 and the ADSs have been quoted on the Nasdaq National Market since October 27, 2000, both under the symbol "CRXL."

The following table sets forth the range of high and low closing prices, in U.S. dollars, for our ordinary shares on the Nasdaq National Market for the periods indicated.

	ADSs	
	High	Low
Annual information for the past five years		
2000	13.63	5.50
2001	12.25	4.88
2002	6.40	2.45
2003	6.16	1.54
2004	13.77	6.38
Quarterly information for the past two years		
2003		
First Quarter	3.18	1.54
Second Quarter	3.45	1.56
Third Quarter	4.35	2.81
Fourth Quarter	6.16	3.81
2004		
First Quarter	8.57	6.38
Second Quarter	9.19	6.86
Third Quarter	8.56	6.83
Fourth Quarter	13.77	8.42
Monthly information for the most recent six months		
October	10.21	8.42
November	12.30	10.03
December	13.77	11.91
January	15.29	12.30
February	14.71	13.23
March	13.84	13.01

Our ordinary shares trade on the Official Market of Euronext Amsterdam N.V. through the book-entry facilities of NEGICEF, Euroclear and Clearstream Luxembourg. For the ordinary shares the International Securities Identification Number (ISIN) code is NL0000358562, the Amsterdam Security Number is 35856 and the Common Code is 11907164.

The following table sets forth the range of high and low closing prices, in euros, for our ordinary shares in The Netherlands for the periods indicated.

	Ordinary Shares	
	High	Low
Annual information for the past five years		
2000	15.45	6.60
2001	13.30	5.40
2002	7.29	2.50
2003	4.92	1.40
2004	10.10	4.83
Quarterly information for the past two years		
2003		
First Quarter	3.00	1.40
Second Quarter	3.04	1.41
Third Quarter	3.82	2.43
Fourth Quarter	4.92	3.28
2004		
First Quarter	6.93	4.83
Second Quarter	7.61	5.62
Third Quarter	7.03	5.65
Fourth Quarter	10.10	6.67
Monthly information for the most recent six months		
October	7.97	6.67
November	9.21	7.85
December	10.1	8.98
January	11.67	9.50
February	11.27	10.18
March	10.57	9.79

Item 10. Additional Information

Memorandum and Articles of Association

Set out below is a summary of material information concerning our shares, which are our ordinary shares together with our priority shares and preference shares, and related material provisions of our articles of association and of Book 2 of the Dutch Civil Code (*Boek 2 van het Burgerlijk Wetboek*). Our articles of association were amended on October 21, 2004, primarily to comply with various provisions of the Dutch Corporate Governance Code. This summary is not complete and is qualified in its entirety by reference to our articles of association and to Dutch law.

General

We were incorporated as a limited liability company (*naamloze vennootschap*) on October 9, 2000 by deed executed before Mr. R.J.J. Lijdsman, civil law notary. Our corporate seat is in Leiden, The Netherlands, and we have offices at Archimedesweg 4, 2333 CN Leiden, The Netherlands. We are registered in the trade register of the Chamber of Commerce and Industry for Leiden under number 28087740. The statement of no objection of the Minister of Justice in respect of our deed of incorporation was issued on October 9, 2000 under number N.V. 1133178. Our agent in the United States is CT Corporation, 111 Eighth Avenue, New York, New York 10011.

Corporate Purpose

Our objects include acquiring, establishing and managing companies in our field, controlling and using intellectual property, and funding our operations.

Management Board and Supervisory Board

Limitation of Liability and Indemnification Matters

Pursuant to Dutch law, each member of our supervisory and management boards is responsible to us for the proper performance of his or her assigned duties. They are also responsible for taking measures to prevent the consequences of any improper performance of duties by another member of our supervisory board or our management board. Our articles of association provide that our managing board members and our supervisory board members are discharged from liability for their actions as board members, if our general meeting of shareholders adopts a resolution to that effect. This discharge extends only to actions or omissions disclosed in or apparent from the adopted annual accounts or otherwise communicated to our general meeting of shareholders.

This discharge of liability may be limited by mandatory provisions of Dutch law, such as in the case of bankruptcy. Under Dutch law, our supervisory board members and members of our management board generally cannot be held personally liable for decisions made exercising their reasonable business judgment.

Our articles of association provide that we shall generally indemnify any person who is or was a member of our supervisory board or our management board or one of our employees, officers or agents, and suffers any loss as a result of any action in connection with their service to us, provided they acted in good faith in carrying out their duties.

This indemnification generally will not be available if the person seeking indemnification acted with gross negligence or willful misconduct in the performance of their duties to us. A court in which an action is brought may, however, determine that indemnification is appropriate nonetheless.

Share Capital

Our authorized share capital amounts to €40,800,002.40 divided into: 85,000,000 ordinary shares, ten priority shares and 85,000,000 preference shares, each with a par value of €0.24.

At December 31, 2004, there were 36,873,421 ordinary shares and ten priority shares issued and outstanding. No preference shares are currently issued and outstanding. The ordinary shares can be issued in bearer or registered form. The priority and preference shares can only be issued in registered form. No share certificates will be issued for shares in registered form.

Ordinary Shares

Our ordinary shares may be in registered or bearer form and will be in bearer form unless the shareholder indicates otherwise in writing. Only bearer ordinary shares can trade on the Amsterdam Stock Exchange.

Bearer Ordinary Shares

All of our bearer ordinary shares will be embodied in a single global share certificate which will not be exchanged for single or multiple physical securities and which we will deposit with NECIGEF for safekeeping on behalf of the parties entitled to the ordinary shares in bearer form.

The ordinary shares represented by the single global share certificate may only be transferred through the book-entry system maintained by NECIGEF. A participant in the collective deposit (verzameldepot) of a securities institution admitted to NECIGEF may, at his own expense, require conversion of one or more of his bearer ordinary shares into ordinary shares in registered form.

Registered Ordinary Shares

We enter holders of registered ordinary shares in the register of shareholders. We do not issue share certificates. However, the shareholder may request an extract from the shareholders' register regarding the ordinary shares registered in his name. We are required to provide this free of charge. Dutch law requires that transfers of registered ordinary shares be recorded in a written instrument to which we are a party or which is served on us, or that the transaction be acknowledged by us.

Priority Shares

All of the issued priority shares are held by Stichting Prioriteit Crucell, also referred to as the Priority Foundation. This foundation was founded in Leiden, The Netherlands on October 25, 2000. The priority shares confer a right to make binding nominations for our supervisory board members. The general meeting can override these binding nominations by a resolution taken by an absolute majority of the votes cast. This vote must represent more than one-third of our issued share capital. Except for the transfer of priority shares to us, priority shares can only be transferred with the approval of our management board and our supervisory board. The board of governors comprises Pieter Strijkert, chairman of our supervisory board, and Martin van Olffen and Joost van Heijningen Nanninga, who are independent members. The board of governors appoints and dismisses its own members. See "Item 6—Directors, Senior Management and Employees".

Preference Shares

As of the date of this annual report, we have not issued any preference shares. On October 25, 2000, we established a foundation called Stichting Preferente Aandelen Crucell, also referred to as the Preferred Foundation. The Preferred Foundation's object is to safeguard our interests and those of our affiliates through acquiring and managing our preference shares and by exercising the rights attaching to these shares, in particular, the voting rights.

We have entered into an agreement with the Preferred Foundation that allows the Preferred Foundation to acquire preference shares up to 50% of the number of our outstanding shares. The Preferred Foundation must pay at least 25% of the nominal value of the preference shares it acquires from us. If we acquire any preference shares, they may be cancelled.

A board of governors of up to five persons directs the Preferred Foundation. Pieter Strijkert, in his capacity as chairman of our supervisory board, and Pieter Bouw, Mick W. den Boogert, Sweder van Wijnbergen and Gerard P. Krans, have been appointed to the board of governors. A majority of these members may not be members or former members of our management or supervisory board, or an employee of any of our advisers, any of our banks or us. These independent members are appointed by the board of governors. The non-independent members are appointed by our supervisory board after consultation with our management board.

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

- voluntary retirement, reaching the age of 72, death or bankruptcy;
- for our non-independent members, resignation, or dismissal by the members of our supervisory board;
- for our independent members, if they cease to be independent;
- dismissal by the complete board of the Preferred Foundation; or
- periodic retirement in accordance with a rotation plan to be drawn up by the Preferred Foundation's board of governors, however, these members may be reappointed.

Other Key Provisions of our Articles of Association

Issue of Shares and Pre-emptive Rights

Our general meeting of shareholders, or our management board if the general meeting of shareholders has delegated the power to it, has the authority to decide on any further issuance of shares or rights to subscribe for shares and on the terms and conditions thereof. Our management board is the authorized corporate body (orgaan) for this purpose until October 9, 2005 and this authorization may at any time be extended for periods of up to five years. Our management board's authority to issue shares is limited to our authorized share capital.

Our management board can issue shares of any class if it has the approval of our supervisory board. Without specific authorization from our general meeting of shareholders our management board may not issue preference shares or grant options for such shares if as a result more preference shares than other shares will or could become outstanding.

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

If our management board has been delegated the authority to issue shares, it can limit or exclude any pre-emptive rights as long as the general meeting of shareholders has granted it that power and our supervisory board approves. At present, our management board is authorized to do this. This authorization is valid until October 9, 2005 and the general meeting of shareholders may at any time extend this authorization for periods of up to five years.

Our shares cannot be issued below par. The priority shares and the ordinary shares must be fully paid up upon issue. Preference shares may be issued without being fully paid up, but at least one-quarter of the nominal amount must be paid up upon subscription, and each issue of preference shares must have the same amount paid up. Our management board may determine the day and the amount of a further call for payment on preference shares.

Acquisition by Us of Shares in Our Own Capital

We may acquire our own shares if the following conditions are met:

- our general meeting of shareholders has authorized our management board to acquire the shares;
- the authorization specifies the number of shares which we may acquire, the manner in which they may be acquired and the limits within which the price must be set;
- our shareholders' equity, after deduction of the price of acquisition, is not less than the sum of the paid and called up portion of the share capital and the reserves that provisions of Dutch law or our articles of association require us to maintain; and
- the aggregate par value of the shares to be acquired, together with the shares in our share capital that we already hold directly, indirectly or as pledgee, does not equal more than one-tenth the aggregate par value of our total issued share capital.

We may not acquire our own shares if they have not been fully paid-up. The authorization by the general meeting of shareholders may be for a term of up to 18 months.

We and our subsidiaries may not vote shares which we or they hold. We may acquire shares to transfer them to our employees or the employees of our group companies under designated stock option plans without authorization.

Capital Reduction

If our management board proposes, our supervisory board approves and Dutch law permits, the general meeting of shareholders can reduce our issued share capital by cancellation of shares or reduction of the nominal value of shares.

Voting Rights and Shareholders' Meetings

We must hold annual general meetings of shareholders within six months of the end of our fiscal year. The annual meeting is held, among other things, to adopt our annual accounts. We must hold extraordinary general meetings of shareholders whenever:

- shareholders and holders of depositary receipts for shares together representing at least one-tenth of our outstanding share capital request it in writing, listing the topics to be discussed; and
- our management board or our supervisory board deems appropriate.

General meetings of shareholders may only be held in the municipalities of Leiden, Amsterdam, Haarlemmermeer (including Schiphol Airport and Schiphol-Rijk), Utrecht, Rotterdam and The Hague.

Each shareholder can attend general meetings in person or by proxy, address the meeting and vote. Each share, whether ordinary, preference or priority, confers one vote on the shareholder. The management board must be notified in writing of a registered shareholder's intention to attend the general meeting of shareholders. The holders of bearer ordinary shares can vote if a NECIGEF

participant sends a written statement as to their shareholdings to our offices. Resolutions are passed by absolute majority of votes cast unless stated otherwise in Dutch law and our articles of association.

The general meeting of shareholders can amend our articles of association, dissolve us, merge us or demerge us only if proposed by the supervisory board.

Dutch law and our articles of association do not impose any limitations on non-Dutch ownership or voting of our ordinary shares.

Annual Accounts

We have a calendar fiscal year. Dutch law requires that within five months after the end of our fiscal year, unless the general meeting of shareholders has extended this period for a maximum of six months, our management board must make available to the shareholders a report with respect to that fiscal year. This report must include the financial statements and a report of an independent accountant. The annual report is submitted to the annual general meeting of shareholders for adoption. See "Management—Limitation of Liability and Indemnification Matters".

Dividends

Annual dividends may only be paid out of profits as shown in the adopted annual financial statements. We may not make distributions if the distribution would reduce our shareholders' equity below certain reserves required by Dutch law or our articles of association. The profits must first be used to set up and maintain reserves required by Dutch law and must then be set off against certain financial losses. The preference and priority shares will be paid their dividends, which will be a certain percentage of their nominal value, first. With supervisory board approval, our management board then decides whether and how much of the remaining profit they will reserve. Any profits remaining can be paid as a dividend on the ordinary shares. With the approval of our supervisory board and subject to Dutch law, our management board can pay an interim dividend. The payment of an interim dividend in our or another entity's shares requires the additional approval of our general meeting of shareholders.

We can make distributions to shareholders at the charge of one or more of our reserves. Holders of shares are entitled to the full dividend for the fiscal year 2000 and subsequent fiscal years. Any dividends that are not claimed within five years of their declaration revert to us.

Amendment of Our Articles of Association and Liquidation Rights

The general meeting of shareholders may only resolve to amend our articles of association or to dissolve, merge or demerge us on the proposal of our supervisory board. The class of shareholders affected must approve a resolution to amend the articles of association to change the rights of the class. If we are dissolved and liquidated, after we pay all debts and liquidation expenses, the holders of preference shares have first rights to payment of any dividends not fully paid to them in previous years and of the nominal value of their preference shares. We must then pay the holders of the priority shares the nominal value of the priority shares. Finally, any remaining assets will be distributed to the holders of ordinary shares.

Enforcement of Civil Liabilities

We are incorporated under the laws of The Netherlands, and the majority of the members of our supervisory board, all of the members of our management board and management team and all of the experts named in this document are residents of, and most of our and their assets are in, jurisdictions outside the United States. As a result, it may not be possible for you to effect service of process within the United States upon us or these persons, or to enforce against us or these persons in courts in the United States, judgments of these courts predicated upon the civil liability provisions of United States

securities laws. In addition, it is not clear whether a Dutch court would impose civil liability on us, members of our management board or supervisory board or management team or any of the experts named in this document in an original action based solely upon the federal securities laws of the United States brought in a court of competent jurisdiction in The Netherlands. Dutch law, furthermore, does not recognize a shareholder's right to bring a derivative action on behalf of a corporation.

Our legal counsel in The Netherlands, Allen & Overy, has advised us that because there is no treaty on the reciprocal recognition and enforcement of judgments in civil and commercial matters between the United States and The Netherlands, courts in The Netherlands will not automatically enforce a final judgment rendered by a United States court. In order to obtain a judgment enforceable in The Netherlands, claimants must litigate the relevant claim again before a Dutch court of competent jurisdiction. Under current practice, however, a Dutch court will recognize a final and conclusive judgment rendered by a United States court if the Dutch court finds that:

- the United States court assumed jurisdiction on grounds which are acceptable from an international law perspective;
- the final judgment results from proceedings compatible with Dutch concepts of due process; and
- the final judgment does not contravene public policy of The Netherlands.

If the Dutch court recognizes the final judgment, that court generally will grant the same judgment without litigating again on the merits.

Material Contracts

On December 18, 2002 we entered into a collaboration agreement with DSM Biologics Holding, Inc., DSM Biologics Company, Inc. and DSM Biologics Company, B.V. Under the terms of the agreement, we grant to DSM an exclusive license to our PER.C6 technology for the contract manufacturing of recombinant proteins and monoclonal antibodies. We will receive licensing fees over a four year period, depending on the achievement of certain cumulative milestones, and are obligated to commit to certain expenditures in connection with the development of the PER.C6 production platform. DSM is entitled to a percentage of all non-service fees under the contract, in addition to an exclusive license to the technology that includes the right to sublicense.

On December 31, 2003, we entered into a collaboration and license agreement with Aventis Pasteur S.A. (now sanofi pasteur) to develop and commercialize influenza vaccine products based on our PER.C6 technology. Under the terms of the agreement, we granted sanofi pasteur an exclusive license to research, develop, manufacture and commercialize influenza vaccine products based on our PER.C6 technology. We received an up-front payment and will receive milestone payments, annual payments, research and development funding totaling €30 million, and high single- up to double-digit royalties on future PER.C6-based influenza vaccine sales. We retain commercialization rights for Japan, where sanofi pasteur will supply finished vaccine products to us and we will pay a royalty on sales to sanofi pasteur.

Exchange Controls

There are currently no Dutch laws, decrees or regulations that restrict the export or import of capital, including, but not limited to, foreign exchange controls, or that affect the remittance of dividends or other payments to non-Dutch residents or to U.S. holders of our securities except as otherwise set forth in Item 10, "Taxation."

Taxation

The following is a summary of the material Dutch and U.S. tax consequences of an investment in ordinary shares or ADSs. This summary does not discuss every aspect of taxation that may be relevant to a particular investor who is subject to special treatment under any applicable law, and is not intended to be applicable in all respects to all categories of investors. This summary also assumes that our business will be conducted in the manner outlined in this document. Changes in our organizational structure or the manner in which we conduct our business may invalidate this summary. The laws upon which this summary is based are subject to change, perhaps with retroactive effect. A change to these laws may invalidate the contents of this summary, which will not be updated to reflect changes in the laws. Prospective investors should consult their professional tax advisors regarding their particular personal tax consequences of acquiring, owning and disposing of our ordinary shares or ADSs.

Certain Dutch Tax Consequences for Holders of Ordinary Shares or ADSs

This summary describes the principal tax consequences that will generally apply in the case of an investment in the ordinary shares or ADSs under Dutch tax laws in force and in effect as of the date hereof, and is subject to changes in Dutch law, including changes that could have retroactive effect. Not every potential tax consequence of such investment under the laws of The Netherlands will be addressed.

Dutch Taxation of Resident Shareholders

The summary of certain Dutch taxes set out in this section "Dutch Taxation of Resident Shareholders" is only intended for the following investors:

- (1) 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 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
- (2) 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 shares or ADSs, excluding:
 - (a) corporate entities that are not subject to Dutch corporate income tax;
 - (b) pension funds (*pensioenfondsen*) and other entities that are wholly or partly exempt from Dutch corporate income tax;
 - (c) 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
 - (d) investment institutions (*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. A deemed substantial interest is present if (part of) a substantial interest has been disposed of, or is deemed to have been disposed of, on a non-recognition basis, unless, in the case of an actual disposal, the consideration received forms part of a substantial interest.

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 "results from other activities."* Under current legislation, the taxable benefit from a Dutch (private) 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 shall be 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. If the actual benefits from the ordinary shares or ADSs exceed 4% of the yield basis, these benefits (capital gains and income) are not taxable.

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 results from other activities, and 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 by a Dutch Individual or to an enterprise 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 results from other activities. 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 held by a Dutch Corporate Entity are generally subject to corporate income tax in its hands.

Withholding Tax. Dividends we distribute generally are subject to a withholding tax imposed by The Netherlands at a rate of 25%. The concept "dividends we distribute" used in this section includes, but is not limited to:

- (1) distributions in cash or in kind, deemed and constructive distributions and repayments of paid-in capital not recognized for Dutch dividend withholding tax purposes;
- (2) 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 recognised for Dutch dividend withholding tax purposes;
- (3) 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, recognised for Dutch dividend withholding tax purposes, has been made or will be made; and
- (4) partial repayment of paid-in capital, recognised for Dutch dividend withholding tax purposes, if and to the extent that there are net profits (*zuivere winst*), unless:
 - (a) the general meeting of our shareholders has resolved in advance to make such repayment; and
 - (b) 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 qualify 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 maintains, directly or indirectly, an interest in the ordinary shares or ADSs.

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 resident in The Netherlands at any time during the ten years preceding the date of the gift or his death. For purposes of the Dutch gift tax, an individual not holding Dutch nationality will be deemed to be resident in The Netherlands if he has been resident in The Netherlands at any time during the twelve months preceding the date of the gift.

Dutch Taxation of Non-Resident Shareholders

This section "Dutch Taxation of Non-resident Shareholders" describes certain Dutch tax consequences for a holder of the ordinary shares or ADSs who is neither resident, nor deemed to be resident, and who has not opted to be treated as a resident in The Netherlands for purposes of Dutch taxation (a "Non-Resident Shareholder").

Withholding Tax. Dividends we distribute generally are subject to a withholding tax imposed by The Netherlands at a rate of 25%. Reference is made to the section "Dutch Taxation of Resident Shareholders—Withholding Tax" for a description of the concept "dividends distributed by us."

If a double taxation convention is in effect between The Netherlands and the country of residence of a Non-Resident Shareholder, such Non-Resident Shareholder may, depending on the terms of that double taxation convention, be eligible for a full or partial exemption from, or refund of, Dutch dividend withholding tax. See the section "Taxation of U.S. Investors—Taxation of Dividends" for a discussion of the partial exemption available under the convention with the United States.

A further condition to avoid "dividend stripping" is that the Non-Resident Shareholder qualifies as the beneficial owner of the dividend. A Non-Resident Shareholder is not considered to be the beneficial owner of the dividend, if the amount of this dividend, following a set of transactions, is ultimately wholly or partly received by another person and this other person also maintains, directly or indirectly, an interest in the ordinary shares or ADSs.

Taxes on Income and Capital Gains. A Non-Resident Shareholder will not be subject to any Dutch taxes on income or capital gains in respect of dividends we distribute (other than the withholding tax described above) or in respect of any gain realised on the disposal of the ordinary shares or ADSs, provided that:

- (1) such Non-Resident Shareholder does not have an enterprise or an interest in an enterprise that is, in whole or in part, carried on through a permanent establishment or a permanent representative in The Netherlands and to which enterprise or part of an enterprise, as the case may be, the ordinary shares or ADSs are attributable; and
- (2) such Non-Resident Shareholder does not have a substantial interest or a deemed substantial interest in us.

Reference is made to the section "Dutch Taxation of Resident Shareholders" for a description of the concepts "substantial interest" and "deemed substantial interest." A Non-Resident Shareholder will furthermore not be subject to any Dutch taxes on income or capital gains in respect of any benefits derived from the ordinary shares or ADSs, if such holder does have an enterprise or an interest in an enterprise that is, in whole or in part, carried on through a permanent establishment or a permanent representative in The Netherlands and the ordinary shares or ADSs are attributable to such enterprise or part of an enterprise, as the case may be, provided that such benefits are exempt under the participation exemption (as laid down in the Dutch Corporate Income Tax Act 1969).

Gift and Inheritance Taxes. No liability for gift or inheritance taxes will arise in The Netherlands with respect to an acquisition of the ordinary shares or ADSs by way of a gift made by, or on the death of, a Non-Resident Shareholder, unless:

- (1) such Non-Resident Shareholder at the time of the gift has or at the time of his death had an enterprise or an interest in an enterprise that is or was, in whole or in part, carried on through a permanent establishment or a permanent representative in The Netherlands and to which enterprise or part of an enterprise, as the case may be, the ordinary shares or ADSs are or were attributable; or
- (2) in the case of a gift of the ordinary shares or ADSs by an individual who at the time of the gift was a Non-Resident Shareholder, such individual dies within 180 days after the date of the gift, while (at the time of his death) being resident or deemed to be resident in The Netherlands.

For purposes of Dutch gift and inheritance tax, an individual who holds Dutch nationality will be deemed to be resident in The Netherlands if he has been resident in The Netherlands at any time during the ten years preceding the date of the gift or his death. For purposes of the Dutch gift tax, an individual not holding Dutch nationality will be deemed to be resident in The Netherlands if he has been resident in The Netherlands at any time during the twelve months preceding the date of the gift.

Capital Tax. Dutch capital tax will be payable by us at a rate of 0.55% on any contribution made to us in respect of the ordinary shares or ADSs, unless an exemption is available.

Other Taxes and Duties. No Dutch registration tax, transfer tax, stamp duty or any other similar documentary tax or duty will be payable in The Netherlands in respect of or in connection with the subscription, issue, placement, allotment or delivery of the ordinary shares or ADSs.

Taxation of U.S. Investors

The following is a summary of the material U.S. federal income tax considerations regarding the purchase, ownership and disposition of ordinary shares or ADSs if you are an eligible U.S. holder. You are an eligible U.S. holder if you are a resident of the United States for purposes of the tax treaty between The Netherlands and the United States and are fully eligible for benefits under the tax treaty. You generally will be entitled to the benefits of the tax treaty if you are:

- the beneficial owner of ordinary shares or ADSs (and of the dividends paid with respect to such ordinary shares or ADSs);
- an individual resident of the United States, a U.S. corporation, or a partnership, estate or trust to the extent your income is subject to taxation in the United States as the income of a resident, in your hands or in the hands of your partners or beneficiaries;
- not resident in The Netherlands for Dutch tax purposes; and
- not subject to an anti-treaty shopping rule.

You generally will not be eligible for the benefits of the tax treaty, and therefore will not be an eligible U.S. holder, if you hold ordinary shares or ADSs in connection with the conduct of business through a permanent establishment, or the performance of services through a fixed base in The Netherlands, or you are not resident in the United States for U.S. tax purposes.

The summary does not purport to be a comprehensive description of all of the tax considerations that may be relevant to your decision to purchase ordinary shares or ADSs. In particular, the summary does not address considerations that may be applicable to you if you will not hold ordinary shares or ADSs as capital assets, or if you are a taxpayer subject to special tax rules, such as a bank, tax-exempt entity, insurance company, a regulated investment company, a pension fund, a real estate investment trust, a dealer in securities or currencies, a person that holds ordinary shares or ADSs as part of an integrated investment (including a "straddle") comprised of ordinary shares or ADSs and one or more other positions, and a person who owns or is deemed to own 10% or more of any class of our stock. The summary is based on laws, treaties and regulatory interpretations in effect on the date of this document, all of which are subject to change. You should consult your own advisers regarding the tax consequences of an investment in the ordinary shares or ADSs in light of your particular circumstances, including the effect of any state, local or other national laws.

We believe that we were a "passive foreign investment company" or "PFIC" for U.S. tax purposes with respect to the year 2004, and also expect to be classified as a PFIC with respect to the year 2005. In order to minimize exposure to unfavorable U.S. tax rules applicable to PFICs, U.S. holders may wish to make a mark-to-market. See "Passive Foreign Investment Company Rules."

For U.S. federal income tax purposes and for purposes of the tax treaty between The Netherlands and the United States, beneficial owners of ADSs will be treated as the owners of the underlying ordinary shares represented by those ADSs.

Taxation of Dividends

Subject to the discussion below under "Passive Foreign Investment Company Rules", the gross amount of dividends distributed by us (including amounts withheld in respect of Dutch withholding tax) generally will be subject to U.S. federal income taxation as foreign source dividend income, and will not be eligible for the dividends received deduction. Subject to certain exceptions for positions that are hedged or held for less than 60 days, an individual U.S. holder generally will be subject to U.S. taxation at a maximum rate of 15% in respect of dividends received after 2002 and before 2009, unless we are in the year prior to the year in which the dividend was paid, and are, in the year in which the dividend is paid, a PFIC. As described above, we believe that we were a PFIC for U.S. tax purposes with respect to the year 2004, and also expect to be classified as a PFIC with respect to the year 2005. Dividends paid in euros will be included in income in a U.S. dollar amount calculated by reference to the exchange rate in effect on the date of receipt by you (or by the depository in the case of ADSs). If such dividends are converted into U.S. dollars on the date of receipt, you generally should not be required to recognize foreign currency gain or loss in respect of the dividend income. If you receive a refund of Dutch withholding tax under the tax treaty between The Netherlands and the United States, you may be required to recognize foreign currency gain or loss to the extent the amount of the tax treaty refund (in dollars) received by you differs from the U.S. dollar equivalent of the refund amount on the date the dividends were received.

You may claim the benefit of the reduced withholding rate of 15 percent that is available under the Tax treaty between The Netherlands and the United States by submitting a duly completed Form IB 92 USA that has been certified by a financial institution (typically the entity that holds the ordinary shares or ADSs as custodian for the holder). If we receive the required documentation prior to the relevant dividend payment date, we may apply the reduced withholding rate at source. If you fail to satisfy these requirements prior to the payment of a dividend, you may claim a refund of the excess of

the amount withheld over the tax treaty rate by filing Form IB 92 USA together with a supplemental statement with the Dutch tax authorities. Pension funds and tax-exempt organizations qualifying for a complete exemption from tax are not entitled to claim tax treaty benefits at source, and instead must file claims for refund by filing Form IB 95 USA.

Subject to applicable limitations and to the special considerations discussed below, Dutch withholding tax at the 15% tax treaty rate will be treated as a foreign income tax that is eligible for credit against your U.S. federal income tax liability or, at your election, may be deducted in computing taxable income. Foreign tax credits will not be allowed for withholding taxes imposed in respect of certain short-term or hedged positions and may not be allowed in respect of arrangements in which your expected economic profit, after non-U.S. taxes, is insubstantial. You should consult your own advisers concerning the implications of these rules in light of your particular circumstances.

Taxation of Capital Gains

Subject to the discussion below under "Passive Foreign Investment Company Rules," gain or loss realized by you on the sale or other disposition of ordinary shares or ADSs will be capital gain or loss in an amount equal to the difference between your basis in the ordinary shares or ADSs and the amount realized on the disposition (or its dollar equivalent, determined at the spot rate on the date of disposition, if the amount realized is denominated in a foreign currency). The gain or loss will be long-term gain or loss if the ordinary shares or ADSs were held for more than one year. The net amount of long-term capital gain recognized by an individual U.S. holder generally is subject to taxation at a maximum rate of 20%; however, net long-term capital gain recognized by an individual U.S. holder after May 5, 2003 and before January 1, 2009 generally is subject to taxation at a maximum rate of 15%.

Passive Foreign Investment Company Rules

Unfavorable U.S. tax rules apply to companies that are considered passive foreign investment companies ("PFICs"). We will be classified as a PFIC in a particular taxable year if either:

- 75% or more of our gross income is treated as passive income for purposes of the PFIC rules; or
- the average percentage of the value of our assets that produce or are held for the production of passive income is at least 50%.

We believe that we were a PFIC in the year 2004, and also expect to be classified as a PFIC in the year 2005.

If we are classified as a PFIC in any year, then a U.S. holder who holds shares during that year and does not make a mark-to-market election will be subject to a special tax at ordinary income tax rates on certain dividends that we pay and on gains realized on the sale of ordinary shares or ADSs ("excess distributions") in all subsequent years, without regard to whether we were a PFIC in the year the excess distribution was received. The amount of this tax will be increased by an interest charge to compensate for tax deferral, calculated as if the excess distributions had been earned ratably over the period the U.S. holder held its ordinary shares or ADSs. Classification as a PFIC may also have other adverse tax consequences, including the denial of a step-up in the basis of ordinary shares and ADSs at death.

You can avoid the unfavorable rules described above by electing to mark your ordinary shares or ADSs to market. For any year in which we are a PFIC, a U.S. holder who makes a mark-to-market election would include as ordinary income the excess of the fair market value of the ordinary shares or ADSs at year-end over the holder's basis in those ordinary shares or ADSs. In addition, any gain

recognized upon a sale of ordinary shares or ADSs would be taxed as ordinary income in the year of sale.

You should consult your own tax advisors regarding the U.S. federal income tax considerations discussed above and the desirability of making a mark-to-market election.

U.S. Backup Withholding Tax and Information Reporting

Payments in respect of the ordinary shares or ADSs that are made in the United States or by a U.S.-related financial intermediary will be subject to information reporting and may be subject to backup withholding unless you:

- are a corporation or other exempt recipient; or
- provide an IRS Form W-9 or an acceptable substitute form, certifying your taxpayer identification number and that no loss of exemption from backup withholding has occurred.

If you are not a U.S. person, you generally are not subject to these rules, but may be required to provide certification of non-U.S. status in order to establish that you are exempt.

Dividends and Paying Agents

Not applicable.

Statement by Experts

Not applicable.

Documents on Display

We are subject to the informational requirements of the Securities Exchange Act of 1934, as amended, and in accordance therewith file information with the U.S. Securities and Exchange Commission ("SEC"). You may read and copy this information at the following location:

Public Reference Room
450 Fifth Street, N.W.
Room 1024
Washington, D.C. 20549

Please call the SEC at 1-800-SEC-0330 for further information on the public reference room. Copies of these materials can also be obtained by mail at prescribed rates from the Public Reference Section of the Securities and Exchange Commission, 450 Fifth Street, N.W., Room 1024, Washington, D.C. 20549. Our ADSs are quoted on the Nasdaq National Market, and consequently, the periodic reports and other information filed by us with the Commission can be inspected at the offices of the Nasdaq National Market, 1735 K Street, N.W., Washington, D.C. 20006. The primary market for our ordinary shares is Euronext Amsterdam. We make our filings with the SEC by electronic means. Any filings we make electronically are available to the public over the internet at the Commission's website at <http://www.sec.gov> and at our website at <http://www.crucell.com>.

Item 11. Quantitative and Qualitative Disclosures about Market Risk

We are exposed to market risk related to changes in interest rates and foreign currency exchange rates between the U.S. dollar and the euro.

Interest Rate Sensitivity

We are exposed to interest rate fluctuations in connection with our cash and cash equivalents that have maturities of less than three months. Substantially all of our cash and cash equivalents consist of bank deposits. We also hold a limited amount of commercial paper issued by European institutions that are at least AA-rated and that have a maturity of less than three months. The securities in our investment portfolio are not leveraged, are classified as available-for-sale and are, due to their very short-term nature, subject to minimal interest rate risk. We currently do not hedge interest rate exposure. Because of the short-term maturities of our investments, we do not believe that an increase in market rates would have any negative impact on the realized value of our investment portfolio.

Foreign Currency Exchange Risk

The majority of our revenue, expense and capital purchasing activities are transacted in Euros. However, since we are party to certain licenses with United States based companies, we are exposed to changes in exchange rates between the euro and the U.S. dollar. Because we receive revenues under U.S. licenses in U.S. dollars, and such revenues are converted to euros for purposes of our financial reporting, we can benefit from a weaker euro and can be adversely affected by a stronger euro relative to the U.S. dollar. Accordingly, changes in foreign exchange rates, and in particular a strengthening of the euro, vis-à-vis the U.S. dollar, may adversely affect our consolidated sales and operating margins as expressed in Euros. We currently do not hedge currency exposure. However, we may hedge currency exposure in the future if we believe it is appropriate to do so.

Item 12. Description of Securities Other than Equity Securities

This item is not applicable.

PART II

Item 13. Defaults, Dividend Arrearages and Delinquencies

None.

Item 14. Material Modifications to the Rights of Security Holders

None.

Item 15. Controls and Procedures

We carried out an evaluation under the supervision and with the participation of our management, including our chief executive officer and chief financial officer, of the effectiveness of the design and operation of our disclosure controls and procedures as of December 31, 2004. There are inherent limitations to the effectiveness of any system of disclosure controls and procedures, including the possibility of human error and the circumvention or overriding of the controls and procedures. Accordingly, even effective disclosure controls and procedures can only provide reasonable assurance of achieving their control objectives. Based upon our evaluation, our chief executive officer and chief financial officer concluded that the disclosure controls and procedures as of December 31, 2004 were effective to provide reasonable assurance that information required to be disclosed in the reports we file and submit under the Securities Exchange Act of 1934, as amended, is recorded, processed, summarized and reported as and when required.

There has been no change in our internal control over financial reporting during 2004 that has materially affected, or is reasonably likely to materially affect, our internal control over financial reporting.

Item 16. Reserved

Item 16A. Audit Committee Financial Expert

The members of our audit committee are all independent, non-executive members of the supervisory board. 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. Notwithstanding the committee members' financial and other experience, the audit committee does not include a "financial expert" as that term is strictly defined in the rules promulgated under the Sarbanes-Oxley Act of 2002.

Item 16B. Code of Ethics

During 2003, we adopted a code of business conduct and ethics that applies to all employees of the Company, including our principal executive officer and principal financial officer. The code of business conduct and ethics has been filed as an exhibit to our Form 20-F for the fiscal year ended December 31, 2003 and can also be accessed on our website at <http://www.crucell.com>. No amendments or waivers of the code of ethics were made or granted during 2004.

Item 16C. Principal Accountant Fees and Services

The Sarbanes-Oxley Act of 2002 requires that audit committees pre-approve all services provided by the Company's independent auditor. This process is critical to the auditor maintaining independence. Our process requires that all services provided by the independent auditor be pre-approved by the audit committee.

During 2003 and 2004 we paid the following amounts to our auditors Ernst & Young for audit services, audit-related services, tax services and other services:

	Year ended December 31,	
	2003	2004
Audit fees	€145	€267
Audit-related fees	29	66
Tax fees	2	—
All other fees	42	—
Total	€218	€333

Audit-related fees

Services include accounting consultations on financial and accounting reporting standards, due diligence services and other attest services.

Tax fees

Services primarily include assistance with expatriate tax compliance.

Other

Services include assistance with grant applications.

Item 16D. Exemptions from the Listing Standards for Audit Committees

Not applicable.

Item 16E. Purchases of Equity Securities by the Issuer and Affiliated Purchasers

Neither we nor any affiliated purchaser have purchased any of our equity securities during the year ended December 31, 2004.

PART III

Item 17. Financial Statements

The registrant has responded to Item 18 in lieu of responding to this item.

Item 18. Financial Statements

See pages F-1 through F-21 of this Form 20-F, included herein.

Item 19. Exhibits

Exhibit Number	Description
1.1	Deed of Incorporation of the Company*
1.2	Amended Articles of Association
4.1	Summary and Lease Agreement dated November 18, 1998, between IntroGene B.V. and Amboz B.V.**
4.2	Summary and Lease Agreement dated November 27, 1997, between IntroGene B.V. and CAM Implants B.V.**
4.3	Lease Agreement dated July 1, 2002 between Crucell Holland B.V. and Oppenheim Property Services B.V. (English translation)***
4.4	Collaboration Agreement dated December 18, 2002 by and between Crucell N.V. and Crucell Holland B.V., and DSM Biologics Holding, Inc., DSM Biologics Company, Inc., and DSM Biologics Company, B.V. (English translation)***†
4.5	Employment Contract dated October 21, 2001 by and between Domenico Valerio and Crucell N.V.***
4.6	Employment Contract dated January 15, 1997 by and between Introgene B.V. (now Crucell Holland B.V.) and R.H.P. Brus
4.7	Employment Contract dated October 25, 2002 by and between Crucell Holland B.V. and Prof. Dr. J. Goudsmit
4.8	Collaboration and License Agreement dated December 31, 2003 by and between Crucell Holland B.V. and Aventis Pasteur S.A. (now sanofi pasteur)†****
8.1	List of Subsidiaries of Crucell N.V.
12.1	Certification of CEO pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
12.2	Certification of CFO pursuant Section 302 of the Sarbanes-Oxley Act of 2002
13.1	Certification of CEO and CFO pursuant to Section 906 of the Sarbanes-Oxley Act of 2002
99.1	Crucell Code of Ethics ****

*

As previously filed with the Securities and Exchange Commission on October 24, 2000 by Crucell N.V. in an Exhibit to the Form F-1.

**

As previously filed with the Securities and Exchange Commission on June 28, 2001 by Crucell N.V. in an exhibit to the Form 20-F.

As previously filed with the Securities and Exchange Commission on April 18, 2003 by Crucell N.V. in an exhibit to the Form 20-F.

As previously filed with the Securities and Exchange Commission on February 27, 2004 in an exhibit to the Form 20-F.

Confidential treatment has been granted with respect to portions of the exhibit indicated by a dagger (†). The omitted portions have been filed separately with the Securities and Exchange Commission.

SIGNATURE

The registrant hereby certifies that it meets all of the requirements for filing on Form 20-F and that it has duly caused and authorized the undersigned to sign this annual report on its behalf.

CRUCELL N.V.

By: /s/ LEONARD KRUIMER

Leonard Kruimer
Chief Financial Officer

Date: April 14, 2005

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REPORT OF INDEPENDENT REGISTERED PUBLIC ACCOUNTING FIRM

The Board of Supervisory Directors and Shareholders of Crucell N.V.

We have audited the accompanying consolidated balance sheets of Crucell N.V. as of December 31, 2004 and 2003, and the related consolidated statements of operations, shareholders' equity and cash flows for each of the three years in the period ended December 31, 2004. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with the standards of the Public Company Accounting Oversight Board (United States). Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. We were not engaged to perform an audit of the Company's internal control over financial reporting. Our audit included consideration of internal control over financial reporting as a basis for designing audit procedures that are appropriate in the circumstances, but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly we express no such opinion. An audit also includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements, assessing the accounting principles used and significant estimates made by management, and evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the consolidated financial statements referred to above present fairly, in all material respects, the consolidated financial position of Crucell N.V. at December 31, 2004 and 2003, and the consolidated results of its operations and its cash flows for each of the three years in the period ended December 31, 2004, in conformity with U.S. generally accepted accounting principles.

/s/ Ernst & Young Accountants

Amsterdam, The Netherlands
January 20, 2005

CRUCCELL N.V.

CONSOLIDATED BALANCE SHEETS

(amounts in thousands)

	December 31, 2004	December 31, 2003
Assets		
Current assets:		
Cash and cash equivalents	€ 76,711	€ 87,210
Trade accounts receivable, net of allowance for doubtful accounts of €240 and €150 at December 31, 2004 and 2003, respectively	2,020	9,547
Prepaid expenses and other current assets	5,424	3,658
Total current assets	€ 84,155	€ 100,415
Notes receivable from employees	224	662
Plant and equipment, net	10,465	11,333
Developed technology, net	4,047	1,996
Total assets	€ 98,891	€ 114,406
Liabilities and shareholders' equity		
Current liabilities:		
Accounts payable	€ 2,108	€ 2,087
Accrued compensation and related benefits	1,050	808
Short term portion of deferred revenue	6,373	5,371
Invoices to receive	1,311	928
Short term portion lease obligations	1,212	1,149
Accrued vacation	688	742
Other accrued liabilities	2,031	631
Total current liabilities	€ 14,773	€ 11,716
Long term liabilities:		
Long term obligation under capital lease	1,385	2,597
Long term portion of deferred revenue	4,198	8,448
Total long term liabilities	€ 5,583	€ 11,045
Shareholders' equity:		
Ordinary shares, €0.24 par value; 85,000,000 shares authorized in 2004 and 89,199,990 shares authorized in 2003; 36,873,421 and 36,006,324 shares issued and outstanding at December 31, 2004 and 2003, respectively	8,850	8,642
Additional paid-in capital	349,167	340,678
Deferred compensation	(4,958)	(4,482)
Accumulated deficit	(274,524)	(253,193)
Total shareholders' equity	€ 78,535	€ 91,645
Total liabilities and shareholders' equity	€ 98,891	€ 114,406

The accompanying notes are an integral part of these financial statements.

CRUCCELL N.V.

CONSOLIDATED STATEMENTS OF OPERATIONS

(amounts in thousands, except share data)

	Year ended December 31,		
	2004	2003	2002
REVENUES:			
License	€ 12,429	€ 4,800	€ 6,664
Service fees	5,712	404	—
Government grants and other	4,481	2,220	2,911
Total revenues	€ 22,622	€ 7,424	€ 9,575
COSTS AND EXPENSES:			
Cost of service fees	5,644	399	—
Research and development	20,468	21,885	24,252
Selling, general and administrative	14,704	7,606	10,386
Developed technology amortization	1,966	1,330	1,331
Goodwill impairment	—	—	30,891
Stock-based employee compensation	2,566	2,696	1,371
Total costs and expenses	€ 45,348	€ 33,916	€ 68,231
LOSS FROM OPERATIONS	(22,726)	(26,492)	(58,656)
Interest income, net	1,503	2,143	3,547
Foreign currency loss	(108)	(19)	(54)
Gain on sale of available for sale securities	—	982	—
Equity in losses of unconsolidated investments	—	—	(507)
NET LOSS BEFORE PROVISION FOR INCOME TAXES	€ (21,331)	€ (23,386)	€ (55,670)
Provision for income taxes	—	—	—
NET LOSS	€ (21,331)	€ (23,386)	€ (55,670)
BASIC AND DILUTED NET LOSS PER SHARE:			
Net loss per share—basic and diluted	€ (0.59)	€ (0.65)	€ (1.57)
Weighted average shares/ADSs outstanding—basic and diluted	36,382,662	35,920,626	35,547,635

The accompanying notes are an integral part of these financial statements.

CRUCELL N.V.
CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
(amounts in thousands of euro, except share data)

	Ordinary shares		Additional Paid-in Capital	Deferred compensation	Accumulated deficit	Total Shareholders equity
	Shares	Amount				
Balance at December 31, 2001	35,318,188	€8,477	€334,708	€(4,334)	€(174,138)	€164,713
Issuance of ordinary shares	331,750	79	915	—	—	994
Deferred compensation	—	—	1,029	(1,029)	—	—
Amortization of deferred compensation	—	—	—	1,371	—	1,371
Net loss	—	—	—	—	(55,670)	(55,670)
Balance at December 31, 2002	35,649,938	€8,556	€336,652	€(3,992)	€(229,807)	€111,409
Issuance of ordinary shares	356,386	86	224	—	—	310
Deferred compensation	—	—	3,186	(3,186)	—	—
Amortization of deferred compensation	—	—	—	2,696	—	2,696
Issuance of warrants to acquire ordinary shares in exchange for services	—	—	616	—	—	616
Net loss	—	—	—	—	(23,386)	(23,386)
Balance at December 31, 2003	36,006,324	€8,642	€340,678	€(4,482)	€(253,193)	€ 91,645
Issuance of ordinary shares	867,097	208	1,201	—	—	1,409
Deferred compensation	—	—	3,042	(3,042)	—	—
Amortization of deferred compensation	—	—	—	2,566	—	2,566
Issuance of warrants and non-employee stock options to acquire ordinary shares in exchange for services	—	—	4,246	—	—	4,246
Net loss	—	—	—	—	(21,331)	(21,331)
Balance at December 31, 2004	36,873,421	€8,850	€349,167	€(4,958)	€(274,524)	€ 78,535

The accompanying notes are an integral part of these financial statements.

CRUCELL N.V.
CONSOLIDATED STATEMENTS OF CASH FLOWS
(amounts in thousands of euro)

	Year ended December 31,		
	2004	2003	2002
Operating activities Net loss	€ (21,331)	€ (23,386)	€ (55,670)
Adjustments to reconcile net loss to net cash used in operating activities:			
Depreciation	2,982	2,712	2,583
Loss on disposal of plant and equipment	—	460	72
Stock based employee compensation	2,566	2,696	1,371
Intangible amortization	1,966	1,330	1,331
Goodwill impairment	—	—	30,891
Equity in losses of unconsolidated investments	—	—	507
Gain on sale of available for sale securities	—	(982)	—
Revenue recognized in exchange for available-for-sale securities	—	(324)	—
Issuance of warrants and non-employee stock options to acquire ordinary shares for services	4,246	616	—
Change in operating assets and liabilities:			
Trade accounts receivable	7,527	(8,538)	2,102
Receivable from related parties and employees	438	239	577
Prepaid expenses and other current assets	(1,767)	(835)	(1,555)
Accounts payable	21	(320)	66
Accrued compensation and related benefits	242	(2,225)	1,289
Deferred revenues	(3,248)	7,787	4,024
Accrued liabilities	972	(1,285)	(88)
Net cash used in operating activities	(5,386)	(22,055)	(12,500)
Cash flow from investing activities			
Purchase of developed technology	(4,017)	—	—
Purchase of plant and equipment	(2,114)	(3,448)	(2,972)
Proceeds from sale of plant and equipment	—	96	—
Proceeds from sale of available for sale securities	—	1,306	—
Net cash used in investing activities	(6,131)	(2,046)	(2,972)
Cash flow from financing activities			
Proceeds from the issuance of ordinary shares	1,409	310	994
Principal payments under capital lease obligation	(1,132)	(902)	(469)
Proceeds from sale and lease-back of plant and equipment	741	1,258	5,349
Net cash provided by financing activities	1,018	666	5,874
Net decrease in cash and cash equivalents	(10,499)	(23,435)	(9,598)
Cash and cash equivalents at beginning of period	87,210	110,645	120,243
Cash and cash equivalents at end of period	€ 76,711	€ 87,210	€ 110,645

The accompanying notes are an integral part of these financial statements.

NOTES TO THE CONSOLIDATED FINANCIAL STATEMENTS

(amounts in thousands of euro, except share data)

Note 1. Business Activities and Basis of Presentation

Crucell N.V. (the "Company"), headquartered in Leiden, the Netherlands, combines three innovative technological platforms to provide powerful and effective means to discover, develop and produce a variety of biopharmaceuticals for the treatment of human diseases. The Company operates in one business segment.

The consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America and include the accounts of the Company and its wholly-owned subsidiaries, Crucell Holland B.V., U-BiSys B.V. and ChromaGenics B.V. Investments in 20% to 50% owned affiliates in which the Company has the ability to exercise significant influence over the investee, but less than a controlling voting interest, are accounted for under the equity method of accounting. All significant intercompany accounts and transactions have been eliminated in consolidation.

On March 11, 2004 Crucell Holland B.V. acquired the outstanding capital stock of ChromaGenics B.V., a privately held biotechnology company based in Amsterdam, the Netherlands. The acquisition has been accounted for as an acquisition of developed technology. The Company paid €4,017 in cash as well as entered into a contingent payment agreement that could result in an additional payment of €7,000 upon receipt of revenues by the Company generated from the STAR technology. After the payments of the contingent consideration, the Company will pay a royalty on revenues generated from the STAR technology through the date the STAR technology patent expires.

Note 2. Summary of Significant Accounting Policies

Risks and Uncertainties and Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States of America requires management to make estimates and assumptions that affect the amounts reported in the financial statements and accompanying notes. Actual results could differ from those estimates.

Revenue Recognition

The Company generates revenues principally from the licensing of its proprietary technology and services performed together with or on behalf of licensees or partners. Under certain arrangements, the Company has no continuing performance obligations after delivery of the associated technology under the license agreement or any other arrangement with the licensee. In such arrangements, initial license fees are recognized as revenue upon persuasive evidence of an arrangement and delivery of the associated technology, which relates to the complete transfer of fully developed technology by the Company and represent the culmination of the earnings process. The Company's arrangements provide for continuing support of its technology at standard consulting rates. Revenues derived from consulting services, which are not essential to licensee's ability to use the Company's technology, are recognized as earned.

In certain arrangements, the Company collaborates with third parties to develop novel products or processes using the Company's proprietary technology. Such arrangements generally include an initial license fee upon the delivery of the Company's proprietary technology and incremental fees for the

Company providing ongoing research and development activities. The research and development activities performed by the Company are substantive and critical to the licensees' exploitation of the delivered technology. Upon persuasive evidence of an arrangement and delivery of the associated technology, the Company recognizes initial fees from such arrangements as revenues over the period of its continuing performance obligations and recognizes fees from research and development activities as revenues when earned. All fees received under the Company's collaboration agreements are non-refundable.

Certain license arrangements provide for additional non-refundable license fees to be paid upon the achievement of milestones. Such additional license fees are recognized as revenue when the amounts become due and payable upon achievement of the milestone.

In addition to the initial fee, the Company's arrangements generally provide that the licensee make semi-annual or annual payments ("license maintenance fees") to maintain the license for a subsequent term. Generally, licensees may terminate the license and related maintenance fees upon 30 days' to 90 days' notice. Annual and semi-annual license maintenance fees are recognized as revenues when the amounts become fixed and payable. The aggregate of annual or semi-annual license maintenance fees paid will generally reduce any royalty payments which may be due based on future product sales of the licensee, if any, under the license agreement. Royalties are recognized as revenue when they become fixed and payable.

The Company receives certain government grants that support the Company's research effort in defined research projects. These grants generally provide for reimbursement of approved costs incurred as defined in various grants. Revenues associated with these grants are recognized when costs under each grant are incurred in accordance with the terms and conditions of the grant and the collectibility of the receivable is deemed probable.

Cost of service fees

Costs of service fees comprise direct labor, materials, and overhead costs.

Research and Development Expenses

Research and development costs are expensed as incurred.

Stock-Based Compensation

The Company accounts for stock-based compensation under the fair value method in accordance with Statement of Financial Accounting Standards (SFAS) No. 123, "Accounting for Stock-Based Compensation." The Company values stock options issued based upon the Black-Scholes option pricing model and recognizes this value as an expense over the period in which the options vest.

Stock compensation expense for options granted to non-employees has been determined in accordance with SFAS No. 123 and Emerging Issues Task Force ("EITF") No. 96-18, "Accounting for Equity Instruments that are Issued to Other than Employees for Acquiring, or in Conjunction with

Selling, Goods or Services," as the fair value of the consideration received or the fair value of the equity instrument issued, whichever is more readily measured.

Income Taxes

The liability method is used in accounting for income taxes. Under this method, deferred tax assets and liabilities are recognized for the tax effect of incurred net operating losses and for tax consequences attributable to differences between the balance sheet carrying amounts of existing assets and liabilities and their respective tax bases. If it is more likely than not that the carrying amounts of deferred tax assets will not be realized, a valuation allowance will be recorded to reduce the carrying amounts of those assets

Deferred tax assets and liabilities are measured using enacted tax rates expected to apply to taxable income in the years in which those temporary differences are expected to be recovered or settled. The effect on deferred tax assets and liabilities of a change in tax rates is recognized in the results of operations in the period that includes the enactment date.

Net Loss Per Share

Basic net loss per share is computed based on the weighted-average number of ordinary shares outstanding during the period. Diluted net loss per share is computed based on the weighted-average number of ordinary shares outstanding, including the dilutive effect of stock options, if any. Basic and diluted net loss per share are the same for all periods presented because the impact of outstanding stock options and warrants is anti-dilutive.

Cash and Cash Equivalents

The Company considers all highly liquid investments with an original maturity of three months or less, which are convertible to a known amount of cash and bear an insignificant risk of change in value, to be cash equivalents.

Long-Lived Assets Other than Goodwill

Plant and equipment is recorded at cost. Depreciation is computed using the straight-line method over the following estimated useful lives: computer equipment, three years; furniture and laboratory equipment, five years; and leasehold improvements, the shorter of the lease term or ten years. Intangible assets other than goodwill consists of developed technology acquired in connection with business combinations in 2000 and the purchase of certain technology in 2004. Developed technology is amortized over five years.

The Company complies with SFAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets," which requires that long-lived assets, other than goodwill, be reviewed for impairment whenever events or changes in circumstances indicate the carrying amount of the assets might not be recoverable. Conditions that would necessitate an impairment assessment include an impairment of goodwill of the associated assets, a significant decline in the observable market value of an asset, a significant change in the extent or manner in which an asset is used, or a significant adverse

change that would indicate that the carrying amount of an asset or group of assets is not recoverable. For long-lived assets to be held and used, the Company recognizes an impairment loss only if its carrying amount is not recoverable through its undiscounted cash flows and measures the impairment loss based on the difference between the carrying amount and fair value. There was no impairment of long-lived assets, including intangible assets other than goodwill, during the three year period ended December 31, 2004.

Goodwill

Effective January 1, 2002, the Company adopted the provisions of SFAS No. 141, "Business Combinations" and SFAS No. 142, "Goodwill and Other Intangible Assets." SFAS 141 requires business combinations initiated after June 30, 2001 to be accounted for using the purchase method of accounting and broadens the criteria for recording intangible assets apart from goodwill. The Company evaluated its goodwill and intangible assets acquired prior to June 30, 2001 using the criteria of SFAS No. 141, which resulted in the remaining unamortized balance of the workforce intangible asset of €3,140 related to a business combination in 2000, being subsumed into goodwill on January 1, 2002. SFAS No. 142 requires that purchased goodwill no longer be amortized, but instead be tested for impairment at least annually. Prior to the adoption of SFAS No. 142, goodwill and the workforce intangible asset were being amortized over five years. The Company performed a transitional impairment test on January 1, 2002, which did not result in the impairment of goodwill.

SFAS 142 prescribes a two-phase process for impairment testing of goodwill. The first phase screens for impairment; while the second phase, if necessary, measures the amount of impairment. The Company completed the first phase of its annual impairment test during the fourth quarter of 2002 and found the carrying value of goodwill to be impaired. During the second phase, the Company determined the full amount of its recorded goodwill of € 30,891 was impaired based upon the excess of the Company's net book value over its market capitalization on the date of testing.

Foreign Currency

The Company's functional currency is the Euro. The Company makes payments primarily in Euro and receives payments in Euro and US dollars. Transaction gains and losses arising from transactions denominated in US dollars and or other non-Euro currencies are included in the Consolidated Statement of Operations under "Foreign currency loss".

Financial Instruments

The Company's financial instruments include primarily cash and cash equivalents, accounts receivable and other current assets, accounts payable, accrued and other liabilities and obligations under capital leases. Due to the short-term nature of the financial instruments, the carrying amounts of these assets and liabilities approximate their fair value.

Concentration of Credit Risk

The Company extends credit based on an evaluation of the customer's financial condition, without requiring collateral. The Company monitors its exposure related to credit losses and maintains allowances for anticipated losses.

Allowance for Doubtful Accounts

The collectibility of accounts receivable is assessed based on a combination of factors. In cases where the Company is aware of circumstances that may impair a specific customer's ability to meet its financial obligations, the Company records a specific allowance against amounts due, and thereby reduces the net recognized receivable to the amount the Company reasonably believes will be collected. For all other customers, the Company recognizes allowances for doubtful accounts based on the length of time the receivables are past due, the current economic conditions and the Company's historical experience. At December 31, 2004 and 2003, the allowance for doubtful accounts reserves was €240 and €150, respectively.

Reclassification

Certain prior year balances have been reclassified to conform to the current year's presentation.

New Accounting Pronouncements

The Company currently prepares its financial statements in accordance with US GAAP and prepares a reconciliation of stockholders' equity, net income and certain other disclosures to Dutch GAAP. In June 2002, the Council of Ministers of the European Union ("EU") approved a new regulation proposed by the European Commission requiring all EU-listed companies, including the Company, to apply International Financial Reporting Standards ("IFRS") in preparing their financial statements for fiscal years beginning on or after January 1, 2005. The Company plans to prepare a reconciliation of stockholders' equity, net income and certain other disclosures from U.S. GAAP to IFRS starting January 1, 2005.

In December 2004, the Financial Accounting Standards Board ("FASB") issued a revision of FASB statement No. 123, Accounting for Stock-Based Compensation ("SFAS No. 123 (R)"). This statement supersedes Accounting Principles Board ("APB") Opinion No. 25, Accounting for Stock Issued to Employees, and its related implementation guidance. SFAS No. 123 (R) addresses the accounting for share-based payment transactions in which a company receives employee services in exchange for either equity instruments of the company or liabilities that are based on the fair value of the company's equity instruments or that may be settled by the issuance of such equity instruments. SFAS No. 123 (R) eliminates the ability to account for share-based compensation transactions using the intrinsic method and generally requires that such transactions be accounted for using a "fair-value"-based method and recognized as expense in the consolidated statement of operations. SFAS No. 123 (R) is effective as of the beginning of the first interim or annual reporting period that begins after June 15, 2005. The Company is currently evaluating the impact of SFAS 123(R) on the Company's consolidated financial statements.

Note 3. Equity Investments

Galapagos Genomics N.V.

In June 1999, the Company together with Tibotec Group N.V., an unrelated party, established a ^{50/50} joint venture, Galapagos Genomics N.V. ("Galapagos"), registered in Mechelen, Belgium to carry out certain functional genomics research activities. In 2002, the company's ownership interest decreased to 20.8%. This investment is accounted for using the equity method, and thus the Company's proportional share of Galapagos' net loss is included in the consolidated statement of operations. The joint venture is engaged in research and development activities and does not have significant revenues, assets or liabilities. In 2002, the Company's proportional share of Galapagos net loss reduced the carrying amount of the investment to zero.

Note 4. Goodwill and Intangible Assets

Goodwill and intangible assets originated from the merger with U-BiSys B.V. in 2000 and from the acquisition of ChromaGenics B.V.'s developed technology in 2004.

The movement of goodwill and intangible assets for the years 2004, 2003 and 2002 is presented below:

	<u>Total</u>	<u>Developed Technology</u>	<u>Workforce</u>	<u>Goodwill</u>
Balance, net, December 31, 2001	€ 35,548	€ 4,657	€ 3,140	€ 27,751
Transfer(1)	—	—	(3,140)	3,140
Impairment	(30,891)	—	—	(30,891)
Amortization	(1,331)	(1,331)	—	—
Balance, net, December 31, 2002	€ 3,326	€ 3,326	€ —	€ —
Amortization	(1,330)	(1,330)	—	—
Balance, net, December 31, 2003(1)	€ 1,996	€ 1,996	€ —	€ —
Purchase of developed technology	4,017	4,017	—	—
Amortization	(1,966)	(1,966)	—	—
Balance, net, December 31, 2004(2)	€ 4,047	€ 4,047	€ —	€ —

(1) The workforce intangible asset was subsumed into goodwill on January 1, 2002 in conjunction with the adoption of SFAS 142.

(2) Developed technology is net of accumulated amortization of €6,623, €4,656, and €3,326 at December 31, 2004, 2003 and 2002, respectively.

The purchase of developed technology in 2004 relates to the acquisition of ChromaGenics B.V. (see Note 1.). The estimated aggregate amortization expense for each of the next respective five years is €1,469, €803, €803, €803, and €169 respectively.

Note 5. Plant and Equipment

Plant and equipment consist of the following:

	December 31,	
	2004	2003
Leasehold improvements	€ 4,204	€ 4,204
Furniture and laboratory equipment	13,541	11,820
Computer equipment	1,534	1,141
	19,279	17,165
Less accumulated depreciation and amortization	(8,814)	(5,832)
Plant and equipment, net	€ 10,465	€ 11,333

At December 31, 2004 and 2003, the Company held laboratory equipment under capital leases with a cost of €4,021 and €3,462, respectively, and a net book value of approximately €2,266 and € 2,691, respectively. Such leases are secured by the value of the underlying assets. Interest expense on lease obligations, which approximates cash payments for interest during the year, was €212, €221 and €146 during the year ended December 31, 2004, 2003 and 2002, respectively.

Note 6. Shareholders' Equity

Share Capital

The Company's authorized share capital amounts to €40,800,002.40 divided into: 85,000,000 ordinary shares, ten priority shares and 85,000,000 preference shares, each with a par value of €0.24. As of December 31, 2004, there were 36,873,421 ordinary shares and ten priority shares issued and outstanding. No preference shares are issued and outstanding as of December 31, 2004.

All of the issued priority shares are held by Stichting Prioriteit Crucell (Priority Foundation). The board of governors comprises of the chairman of the Company's supervisory board and two other independent members. The Priority Foundation is able to make binding nominations for the supervisory board members. The general meeting of shareholders can override these votes by an absolute majority of the votes cast, which must represent more than one-third of the Company's issued share capital.

All of the preference shares are held by a foundation called Stichting Preferente Aandelen Crucell (Preferred Foundation). The board of governors comprises of the Company's chairman of the supervisory board and four other independent members. The preference shares are held by the Preferred Foundation in which the Company has entered into an agreement that allows it to acquire preference shares up to 50% of the number of outstanding shares. The Preferred Foundation must pay at least 25% of the nominal value of the preference shares it acquires from the Company. If any preference shares are acquired by the Company they must be cancelled.

Repurchase of Shares

Pursuant to a resolution of the shareholders, the Company may repurchase up to 10 percent of its outstanding share capital through December 3, 2005.

Stock Option Plan

The Company maintains a stock option plan whereby the remuneration committee of the supervisory board may grant options to employees, directors and members of the supervisory board. All options are exercisable immediately upon grant. Upon exercise of the options, employees are subject to profit–retribution provisions. Such provisions entitle the Company to receive a portion of the profits upon the sale of the shares, calculated as the difference between the total proceeds from the sale of shares and the aggregate exercise price. The portion of the profits payable to the Company decreases ratably over three to four years. The relevant portion of any profits derived by the employee from the sale of shares received on exercise of options must be remitted to the Company if the employee terminates employment prior to the end of the relevant period.

The options expire four to eight years from the date of grant, or earlier upon termination of employment with the Company. Upon termination of employment with the Company, options must be exercised within 90 days. Generally, options granted under the stock option plan are granted at exercise prices which exceed the fair value of the Company's ordinary shares at the date of grant.

In accordance with the terms of a cash bonus plan, if an employee maintains continuous employment with the Company for a period of four years, and defers exercising awarded options until the last month of the option term, the employee receives a cash bonus. The Company recognizes compensation expense ratably during the employment period required under the cash bonus plan. In 2003, the cash bonus plan was eliminated for certain employees resulting in a reduction to compensation expense of approximately €2,300.

In January 2003, the supervisory board approved a new option plan whereby previously awarded options to employees and members of the supervisory board with an exercise price of €21.00 per share could be exchanged for an equal number of new options (the "replacement options"). The replacement options have an exercise price of €3.49, which was 161% of the average closing stock price of the Company on the three days preceding the option grant date, and have an eight year life. The replacement options are exercisable immediately, but are subject to profit retribution provisions. Such provisions entitle the Company to receive a portion of the profits upon the sale of the shares, calculated as the difference between the total proceeds from the sale of shares, and the aggregate selling price. The portion of the profits payable to the Company decreases ratably over three years. The relevant portion of any profits derived by the employee from the sale of shares received on exercise of options must be remitted to the Company if the employee terminates employment prior to the end of the three year period. A total of 1,295,650 options with an exercise price of €21.00 per share were replaced under the new option plan, resulting in incremental deferred compensation of €1,516 or €1.17 per option. Compensation expense is recognized ratably over a period of three years.

Options issued subsequent to January 2003 are subject to the terms of the new option plan. Options issued under this option plan have an eight year life and will be issued at exercise prices equal to 161% of the average closing stock price of the Company on the three days preceding the option grant date. The options are immediately exercisable, and are subject to profit retribution provisions which lapse over a period of three years.

In May 2003, the supervisory board approved amendments to the terms of outstanding and future options held by members of the management board, which include the Company's chief executive

officer, chief financial officer, chief operating officer and chief scientific officer, whereby, following a change of control resulting in termination of employment, members of the management board may exercise options over the shorter of a three year period or the remaining term of the options.

In December 2003, the terms of all outstanding stock options to the supervisory board were modified such that options vest immediately and are no longer subject to profit retribution provisions. The Company recognized compensation expense of €495 representing the total amount of deferred compensation associated with options held by members of the supervisory board.

In April 2004, the supervisory board approved a new option plan whereby employees and members of the supervisory board are granted options with an exercise price 126% greater than the average closing stock price of the Company on the three days preceding the option grant date and have a five year life. The options are subject to profit retribution provisions. Such provisions entitle the Company to receive a portion of the profits upon the sale of the shares, calculated as the difference between the total proceeds from the sale of shares, and the aggregate selling price. The portion of the profits payable to the Company decreases ratably over three years. The relevant portion of any profits derived by the employee from the sale of shares received on exercise of options must be remitted to the Company if the employee terminates employment prior to the end of the three-year period. Compensation expense is recognized ratably over a period of three years.

Total compensation cost recognized for all stock-based employee compensation awards was €2,566, €2,696 and €1,371 in 2004, 2003 and 2002 respectively.

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

	<u>Number of options</u>	<u>Weighted average exercise price</u>
Balance at December 31, 2001	4,620,264	9.43
Granted	443,500	5.48
Exercised	(331,750)	3.00
Forfeited	(202,850)	14.95
	<hr/>	
Balance at December 31, 2002	4,529,164	9.27
Granted	2,512,554	4.19
Exercised	(356,386)	0.87
Forfeited	(2,326,574)	13.63
	<hr/>	
Balance at December 31, 2003	4,358,758	4.70
Granted	1,333,500	9.59
Exercised	(867,097)	1.62
Forfeited	(6,150)	8.48
	<hr/>	
Balance at December 31, 2004	4,819,011	6.42

Included in the options outstanding as of December 31, 2004 are options to acquire 696,679 ordinary shares that are held by former employees. These employees have been permitted to continue vesting in these options for services rendered.

The following table summarizes information about the Company's stock options outstanding at December 31, 2004:

Exercise price	Outstanding Options at December 31, 2004	Weighted average remaining contractual life (years)	Exercisable options
€0.49–€3.00	243,969	4.06	243,969
€3.01–€5.00	1,720,600	5.67	1,720,600
€5.01–€7.00	899,604	5.59	899,604
€7.01–€11.66	1,954,838	3.18	1,954,838
Total	4,819,011		4,819,011

As of December 31, 2004, a total of 5,531,013 ordinary shares have been reserved for issuance under the option plan, of which 4,819,011 are subject to outstanding options (including non–employee stock options).

The Company accounts for its employee stock options under the fair value method in accordance with SFAS No. 123, "Accounting for Stock–Based Compensation". The fair value of options was estimated at the date of grant using the Black–Scholes option pricing model, with the following weighted average assumptions:

	Year ended December 31,		
	2004	2003	2002
Risk–free interest rate	2.9%	2.5%	4.5%
Expected dividend yield	—	—	—
Expected volatility	62.3%	87.0%	93.0%
Expected life (years)	4.0	4.0	4.0

The weighted average fair value of options granted during the years ended December 31, 2004, 2003 and 2002 was €3.28, €1.41 and €3.01, respectively.

Warrants

In 2003, the Company granted warrants to acquire 250,000 ordinary shares with an exercise price of €3.00 per share to a consultant in exchange for services. The warrants were earned by the consultant over the service period which ended in 2004, and expire in July 2008.

Note 7. Commitments and Contingencies

Total minimum payments under non-cancelable operating leases and capital leases are as follows at December 31, 2004:

	Capital Leases	Operating Leases
2005	€ 1,345	€ 1,838
2006	1,036	1,254
2007	407	1,220
2008	—	1,218
2009	—	1,218
Thereafter	—	2,537
Total minimum payments	2,788	€ 9,285
Less interest	(191)	
Present value of minimum lease payments	2,597	
Less current portion	(1,212)	
Long term portion of capital lease obligations	€ 1,385	

Rental expense was €1,174, €1,165 and €1,377 for the years ended December 31, 2004, 2003 and 2002, respectively.

The Company has future minimum payments under non-cancelable research and licensing agreements whereby it is obligated to make payments of €1,828, €1,804, and €1,519 in 2005, 2006, and 2007 respectively, with no required minimum payments thereafter.

Certain lease agreements contain provisions whereby the Company is required to make immediate payment of all amounts due under the lease in the event the Company's cash and cash equivalents balance falls below € 25,000 or stockholders' equity or cash equivalents falls below € 75,000. At December 31, 2004, €3,880 of amounts due under leases is subject to this provision.

The Company also has other bank guarantees that amount to €1,315 at December 31, 2004.

The Company is party to claims and litigation incidental to the business. The Company believes the ultimate resolution of these matters will not have a material adverse effect on its financial position, results of operations, or cash flows.

Note 8. Collaboration Agreements

In December 2002, the Company entered into a collaboration agreement with DSM Biologics ("DSM") pursuant to which the Company granted DSM an exclusive license to use Crucell's PER.C6 platform for the contract manufacturing of recombinant proteins and monoclonal antibodies. Under the terms of this agreement, the Company receives licensing fees over a four year development period and is obligated to commit certain expenditures in connection with the development of the PER.C6 production platform. Under the terms of the arrangement, DSM is entitled to a percentage of all non-service fees received by the Company from third parties licensing the Company's PER.C6 technology in certain fields, in addition to an exclusive license to the technology that includes a right to

sub-license. In December 2002, the Company received an up-front non-refundable licensee fee and in June 2004 the Company received a non-refundable milestone payment. Additional payments from DSM may be triggered upon certain dates and the attainment of certain milestones. Due to the Company's continuing performance obligations related to the novel use of its technology during the development period, the up-front license fee was initially recognized as deferred revenue and is being recognized as revenue ratably over four years, the estimated period of development. Milestones, related to scientific and technical achievements are recognized as revenue when the milestone is obtained.

In December 2003, the Company entered into a collaboration and license agreement with Aventis Pasteur S.A. (as of 2004 sanofi pasteur S.A. ("Sanofi")) pursuant to which Sanofi received an exclusive license to research, develop and manufacture influenza vaccines based on the Company's PER.C6 technology. Under the terms of the agreement the Company is obliged to provide research and development. In addition, the Company is entitled to milestone payments, annual minimum royalty payments, research and development funding, and royalties upon the development of a PER.C6-based influenza vaccine. The Company retains the commercialization rights in Japan, whereby the Company can request Sanofi to supply finished vaccine products to the Company, where royalties will be due to Sanofi. Due to the Company's continuing performance obligations related to the novel use of its technology during the development period, the up-front license fee has been deferred and will be recognized as revenue ratably over the estimated development period of three years. Minimum annual royalties during the development period, which are creditable against future royalties, are recognized as revenue when earned. Milestones, related to scientific and technical achievements are recognized as revenue when the milestone is obtained. Service fees for work performed under the collaboration agreement are recognized when earned.

The Company maintains a defined contribution plan in The Netherlands whereby participants may contribute up to 12% of their pre-tax base salaries, subject to certain limitations. The Company makes a matching contribution equal to 100% of an employee's pre-tax contributions. The contributions to the plan were €1,032, €761 and €525 for the years ended December 31, 2004, 2003 and 2002, respectively.

Note 10. Revenues

The table below reflects the geographical composition of revenues for the years ending December 31, 2004, 2003 and 2002.

	Year ended December 31,		
	2004	2003	2002
Europe	10,042	€2,310	€3,072
North America	12,535	5,051	6,347
Asia	45	63	156
	€22,622	€7,424	€9,575

The Company had two individual customers whose respective accounts receivable balances represented 36% and 23% of the Company's total accounts receivable balance as of December 31, 2004.

Note 11. Income Taxes

The Company has tax loss carry forwards of €85,766, €68,802 and €55,289 at December 31, 2004, 2003 and 2002 respectively. The Company has evaluated evidence impacting the realizability of its deferred tax assets, which consist principally of tax loss carry forwards. Management has considered the Company's history of net losses and concluded that it is more likely than not that the full benefits of these tax loss carry forwards will not be realized in the near term. Accordingly, the Company recorded a valuation allowance equal to 100% of the net deferred tax asset balance at December 31, 2004, 2003 and 2002.

Tax losses may be carried forward indefinitely and offset against future taxable profits. On January 1, 2001, a bill was enacted that may limit the ability to offset losses against future profits when the beneficial ownership of a company changes. This new law could limit the Company's ability to realize the benefits of its tax loss carry forward in the future.

Note 12. Significant Customers

A summary of significant customers based on a percentage of total revenues is as follows:

	<u>2004</u>	<u>2003</u>	<u>2002</u>
Customer A	26%	(*)	(*)
Customer B	23%	17%	(*)
Customer C	(*)	15%	15%
Customer D	(*)	(*)	13%
Customer E	(*)	(*)	11%
	<u>49%</u>	<u>32%</u>	<u>39%</u>

(*) Revenue less than 10% of total revenues.

Note 13. Quarterly Financial Data (Unaudited)

The following is a summary of the quarterly results of operations for the fiscal years ended December 31, 2004, 2003, and 2002.

	<u>Fiscal year 2004 (unaudited)</u>			
	<u>Q1</u>	<u>Q2</u>	<u>Q3</u>	<u>Q4</u>
Revenues	€ 4,005	€ 8,015	€ 4,098	€ 6,504
Loss from operations	(7,396)	(2,476)	(5,857)	(6,997)
Net loss before provision for income taxes	(7,047)	(2,043)	(5,475)	(6,766)
Net loss	(7,047)	(2,043)	(5,475)	(6,766)
Net loss per share basic and diluted	(0.19)	(0.06)	(0.15)	(0.18)

	<u>Fiscal year 2003 (unaudited)</u>			
	<u>Q1</u>	<u>Q2</u>	<u>Q3</u>	<u>Q4</u>
Revenues	€ 2,120	€ 1,146	€ 1,192	€ 2,966
Loss from operations	(4,318)	(6,795)	(8,608)	(6,771)
Net loss before provision for income taxes	(3,629)	(6,227)	(7,179)	(6,351)
Net loss	(3,629)	(6,227)	(7,179)	(6,350)
Net loss per share basic and diluted	(0.10)	(0.17)	(0.20)	(0.18)

	<u>Fiscal year 2002 (unaudited)</u>			
	<u>Q1</u>	<u>Q2</u>	<u>Q3</u>	<u>Q4</u>
Revenues	€ 2,161	€ 2,853	€ 2,003	€ 2,558
Loss from operations	(5,861)	(6,945)	(7,426)	(38,424)
Net loss before provision for income taxes	(5,292)	(6,144)	(6,546)	(37,688)
Net loss	(5,292)	(6,144)	(6,546)	(37,688)
Net loss per share basic and diluted	(0.15)	(0.17)	(0.18)	(1.07)

Note 14. Net Loss and Shareholders' Equity under Accounting Principles Generally Accepted in The Netherlands

The consolidated financial statements have been prepared in accordance with generally accepted accounting principles in the United States of America ("U.S. GAAP"), which differ in significant respects from generally accepted accounting principles in The Netherlands ("Dutch GAAP"). The tables below reconcile the net loss and shareholders' equity of the Company under U.S. GAAP to the net loss and shareholders' equity under Dutch GAAP:

	Year ended December 31,		
	2004	2003	2002
Net loss under U.S. GAAP	€ (21,331)	€ (23,386)	€ (55,670)
Intangible assets	1,330	1,330	32,222
Stock option compensation	5,320	3,312	1,371
Revenue recognition	(4,250)	7,750	4,948
Equity in result of joint venture	(704)	1,347	1,481
Net loss under Dutch GAAP	€(19,635)	€(9,647)	€(15,648)

	Year ended December 31,	
	2004	2003
Shareholders' equity under U.S. GAAP	€ 78,535	€ 91,645
Intangible assets	(666)	(1,996)
Revenue recognition	8,448	12,698
Equity in result of joint venture	2,124	2,828
Shareholders' equity under Dutch GAAP	€88,441	€105,175

The following accounting principles were followed by the Company pursuant to Dutch GAAP:

Intangible assets

Intangible assets consist of the capitalization of start-up expenses, certain research and development activities and goodwill. Such intangible assets are amortized over their estimated useful life.

Stock option compensation

In case of a grant of stock options below the market value of the underlying shares the difference will be included in the profit and loss account. Stock compensation expense for options granted is determined at the intrinsic value (difference between the market value upon date of grant and the exercise price of the option).

Revenue recognition

Revenue is recognized upon persuasive evidence of an arrangement.

Equity in result of joint venture

The result is recognized based upon the ownership interest in the equity value at year-end of the joint venture.

Note 15. Subsequent events (Unaudited)

On March 9, 2005 the Company announced that Galapagos is considering a Euronext stock exchange listing in 2005. The primary reason for the listing is to raise additional funds to enhance Galapagos' drug discovery operations, which are predominantly aimed at developing breakthrough medicines for the bone and joint diseases—osteoarthritis, osteoporosis and rheumatoid arthritis.

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Exhibit 1.2

STATEMENT ABOUT ARTICLES OF ASSOCIATION

Robert Jan Jozef Lijdsman, civil law notary in Amsterdam, the Netherlands,

hereby declares:

the attached document is a fair English translation of the Articles of Association of:

Crucell N.V.,
having its official seat in Leiden,

as they read after execution of the deed of amendment on 21 October 2004 before R.J.J. Lijdsman, civil law notary aforementioned, with respect to which amendment a ministerial Statement of No Objections was granted on 16 June 2004, under number NV 1133178.

Crucell N.V. is a public limited liability company under Dutch law (*'naamloze vennootschap met beperkte aansprakelijkheid'*), having its office address at Archimedesweg 4, 2333 CN Leiden, the Netherlands, and registered in the Commercial Register under number 28087740.

In preparing the attached document, an attempt has been made to translate as literally as possible without jeopardising the overall continuity of the text. Inevitably, however, differences may occur in translation, and if they do, the Dutch text will by law govern.

In the attached document, Dutch legal concepts are expressed in English terms and not in their original Dutch terms; the concepts concerned may not be identical to concepts described by the English terms as such terms may be understood under the laws of other jurisdictions.

Amsterdam, 21 October 2004.

[SEAL]

ARTICLES OF ASSOCIATION

(Crucell N.V.)

CHAPTER I. DEFINITIONS.

Article 1.

In these Articles of Association the following terms shall have the following meanings:

- **"Euronext Listing Rules"** means the rules relating to securities (*'Fondsenreglement'*) of Euronext Amsterdam N.V. in Amsterdam, including any changes thereof from time to time.
- **"Euronext Official Price List"** means the Official Price List (*'Officiële Prijzlijst'*) of Euronext Amsterdam N.V. in Amsterdam or any publication replacing such Official Price List.
- **"AGM"** means the General Meeting of Shareholders held for the purpose of dealing with the annual accounts and the annual report.
- **"Board of Management"** means the management board of the Company.
- **"Company"** means the company the internal organisation of which is governed by these Articles of Association.
- **"Distributable Equity"** means that part of the Company's equity which exceeds the aggregate of the part of the capital which has been paid-up and called and the reserves which must be maintained by virtue of the law or these Articles of Association.
- **"General Meeting"** means the body of the Company formed by Shareholders and other Persons entitled to vote.
- **"General Meeting of Shareholders"** means a meeting of Shareholders (or their representatives) and other Persons entitled to attend such meetings.
- **"Group Company"** means a legal entity or company with which the Company is connected in a group within the meaning of Section 2:24b of the Dutch Civil Code.
- **"Necigef"** means 'Nederlands Centraal Instituut voor Giraal Effectenverkeer B.V.', being the 'central institution' (*'centraal instituut'*) as referred to in the Dutch Securities Depository Act (*'Wet giraal effectenverkeer'*).
- **"Necigef-beneficiary"** means, in respect of the ordinary shares, a participant (*'deelgenoot'*) in the collective deposit (*'verzameldepot'*) of ordinary shares of a Necigef-participant, all within the meaning of the Dutch Securities Depository Act.
- **"Necigef Global Certificate"** means the one single share certificate representing all bearer ordinary shares in issue from time to time referred to in Article 5, paragraph 2, of these Articles of Association.
- **"Necigef-participant"** means an institution which is an 'associated institution' (*'aangesloten instelling'*) within the meaning of the Dutch Securities Depository Act.
- **"Person"** means any individual, partnership, corporation, unincorporated organisation or association, limited liability company, trust or other natural person or legal entity.
- **"Priority"** means the body of the Company formed by the holder or holders (as the case may be) of priority shares.
- **"Shareholder"** means a holder of one or more shares in the capital of the Company.

- "Subsidiary" means (i) a legal entity in which the Company or one or more of its Subsidiaries, whether or not by virtue of agreement with other Persons who can cast votes, can exercise alone or together more than half of the voting rights in the general meeting of members or shareholders of that legal entity; or (ii) a legal entity in respect of which the Company or one or more of its Subsidiaries is a member or shareholder and, whether or not by virtue of agreement with other Persons who can cast votes, alone or together, can appoint or dismiss more than half of the managing directors or the supervisory directors, also in the event all those who can cast votes, vote; or (iii) another Subsidiary of the Company as defined in Section 2:24a of the Dutch Civil Code.

- "Supervisory Board" means the supervisory board of the Company.

- "Supervisory Director" means a member of the Supervisory Board.

CHAPTER II. NAME, OFFICIAL SEAT AND OBJECTS.

Article 2. Name and Official Seat.

2.1

The name of the Company is: **Crucell N.V.**

2.2

The Company's official seat is Leiden.

Article 3. Objects.

The objects of the Company are:

a.

the incorporation and acquisition of, participation in, co-operation with, conducting the management of and the financing of other companies and enterprises, particularly companies or enterprises active in the biological and industrial technology in general and more in particular in the development, testing, upgrading and operation of bio-pharmaceutical procedures and the development, evaluation and exploitation of clinical applications of such procedures and bio-pharmaceuticals;

b.

the acquisition, administration, ownership, control, exploitation and alienation of registered property, membership of associations and co-operative associations which have as object the exploitation of registered property, securities, industrial and intellectual property rights, non-registered property and other components of equity capable of being a source of income, the investment of money and other value in the aforementioned goods, the brokerage of the mentioned transactions and the lending and borrowing of funds, whether under the security of a mortgage or not;

c.

the provision of collateral for the debts and other obligations, including for the debts and obligations of the Company or of other companies or of other companies or enterprises with which the Company is affiliated in a group or of third parties;

as well as to do all that is connected therewith or may be conducive thereto, all to be interpreted in the broadest sense.

CHAPTER III. CAPITAL AND SHARES; REGISTER OF SHAREHOLDERS.

Article 4. Authorised Capital. Classes of Shares.

4.1

The Company's authorised capital equals forty million eight hundred thousand two euro and forty euro cent (EUR 40,800,002.40).

4.2

It is divided into:

- eighty-five million (85,000,000) ordinary shares with a nominal value of twenty-four eurocent (EUR 0.24) each;
- ten (10) priority shares with a nominal value of twenty-four eurocent (EUR 0.24) each; and
- eighty-five million (85,000,000) preference shares with a nominal value of twenty-four eurocent (EUR 0.24) each.

4.3

The ordinary shares may, at the option of the Shareholder, be registered shares or bearer shares. The priority shares and preference shares shall be registered shares. No share certificates shall be issued for registered shares.

4.4

Wherever these Articles of Association refer to shares or Shareholders, such terms shall be understood to refer to all classes of shares mentioned in paragraph 2 and the holders thereof, unless the contrary is apparent from the context.

4.5

The Company may co-operate in the issuance of depositary receipts for its shares. Holders of depositary receipts issued for shares in the Company with the Company's co-operation shall have the rights conferred to them by law, also to the extent such rights are not expressly referred to in these Articles of Association.

Article 5. Bearer Ordinary Shares: Necigef Global Certificate.

5.1

On the occasion of the issuance of ordinary shares the Person becoming entitled to receive such share may request the Company, in writing, to deliver a registered ordinary share. Without such request, the Person entitled to such share shall obtain a bearer ordinary share in conformity with the provisions of this Article 5.

5.2

All bearer ordinary shares in issue from time to time shall be represented by one single share certificate (the "*Necigef Global Certificate*").

5.3

The Necigef Global Certificate is intended to be held on behalf of the party or parties entitled to it by Necigef.

5.4

Without prejudice to the provisions in Article 40, paragraph 5, of these Articles of Association, Necigef shall be irrevocably charged with the management of the Necigef Global Certificate in its capacity as controller of the relevant book-entry deposit of the ordinary shares.

5.5

As soon as the share certificate has been taken into custody by Necigef (a) Necigef will credit each Necigef-participant that has been nominated by one or more parties entitled to shares with a share in the book-entry deposit of the shares proportional to the right of the party or parties entitled to shares and (b) each Necigef-participant that has been nominated by one or more parties entitled to shares shall correspondingly credit such party or parties in the collective deposit of the shares at that Necigef-participant.

5.6

In the event of any subsequent issue of shares (a) on request by the Company Necigef will inscribe or have inscribed the newly issued shares on the certificate embodying the shares as a result of which the number of shares embodied in that certificate shall be increased by the number of shares so inscribed, and (b) will credit each Necigef-participant nominated by one or more parties entitled to shares with a share in the book-entry deposit of the shares proportional to the right of the party or parties entitled and (c) each Necigef-participant nominated by one or more parties entitled to shares shall correspondingly credit such party or parties in the collective deposit of the shares at that Necigef-participant

5.7

If a Necigef–beneficiary wishes to take delivery of one or more ordinary shares not exceeding in number the quantity represented by his co–ownership, (a) Necigef will write ordinary shares off or have ordinary shares written off the Necigef Global Certificate such that the number of ordinary shares embodied in the Necigef Global Certificate shall be decreased by the number of ordinary shares so written off (b) Necigef in its capacity as controller of the book–entry deposit of the ordinary shares shall deliver the ordinary shares by deed of transfer to the party or parties entitled and report the delivery or have it reported to the Company or have the Company acknowledge the delivery (c) Necigef shall correspondingly debit the share in the name of the relevant Necigef–participant in the book–entry deposit of the ordinary shares and (d) the relevant Necigef–participant shall debit the party entitled in the collective deposit of the ordinary shares at that Necigef–participant and (e) the Company will enter the party entitled in its register of shareholders as holder of the registered ordinary shares delivered to him.

5.8

If a party entitled to one or more ordinary registered shares wishes such ordinary shares to be converted into bearer shares, then (a) the party entitled shall deliver the ordinary share or ordinary shares to Necigef by deed of transfer and Necigef shall report the delivery or have it reported to the Company or have such delivery acknowledged by the Company and (b) the Company shall remove the party entitled from the register of shareholders as holder of the ordinary share or ordinary shares and (c) Necigef shall inscribe or have inscribed the ordinary share or ordinary shares on the Necigef Global Certificate so that the number of ordinary shares embodied in the Necigef Global Certificate shall be increased by the number so inscribed and (d) Necigef will credit the Necigef–participant nominated by the party entitled to a share in the book–entry deposit of the shares proportional to the number of shares inscribed on the Necigef Global Certificate and (e) the Necigef–participant will credit the party entitled correspondingly in the collective deposit of the shares at that Necigef–participant.

5.9

For the purpose of application of the provisions of these Articles of Association, Shareholders shall be understood to include Necigef–beneficiaries.

Article 6. Register of Shareholders.

6.1

The Board of Management shall keep a register containing the names and addresses of all holders of registered shares, with reference to the class of shares.

6.2

Every holder of one or more registered shares and any Person having a right of usufruct or a right of pledge over one or more such shares shall be obliged to provide the Company in writing with their address.

6.3

A member of the Board of Management shall sign all entries and notes in the register of Shareholders or another Person authorised to do so by the Board of Management.

6.4

Section 2:85 of the Dutch Civil Code also applies to the register.

6.5

Upon his request, a Shareholder shall be provided with written evidence of the contents of the register with regard to the shares registered in his name, free of charge, and the statement so issued may be validly signed on behalf of the Company by a Person to be designated for that purpose by the Board of Management. Such extract from the register is for information purposes only and not marketable.

CHAPTER IV. ISSUANCE OF SHARES.

Article 7. Body Competent to Issue Shares.

7.1

Shares shall be issued pursuant to a resolution of the Board of Management. The resolution shall be subject to the approval of the Supervisory Board. This authority of the Board of Management

shall relate to all unissued shares of the Company's authorised capital, as applicable now or at any time in the future. The duration of this authority shall be established by a resolution of the General Meeting and shall be for a period of maximum five years, without prejudice to the provisions of Article 46 of these Articles of Association.

7.2

Designation of the Board of Management as the company body competent to issue shares may be extended by amending these Articles of Association or by a resolution of the General Meeting for a period not exceeding five years in each case. The resolution of the General Meeting shall be subject to the approval of the Supervisory Board. The number of shares that may be issued shall be determined at the time of this designation. Designation by resolution of the General Meeting cannot be revoked unless determined otherwise at the time of designation.

7.3

Upon termination of the authority of the Board of Management, the issue of shares shall thenceforth require a resolution of the General Meeting, save where another company body has been designated by the General Meeting. The resolution of the General Meeting to issue shares or to designate another company body shall be subject to the approval of the Supervisory Board.

7.4

The Board of Management is authorised, subject to the approval of the Supervisory Board, in the event of a merger of a Subsidiary, to issue ordinary shares at the charge of one or more of the Company's reserves (which do not have to be maintained by law or under these Articles of Association), in as far as the Board of Management has been designated as the company body competent to issue shares.

7.5

The 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 issued preference shares would be effected which would exceed one hundred per cent (100%) of the amount of issued ordinary and priority shares may only be effected after the General Meeting has for the specific instance granted its concurrence.

7.6

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 does not exceed one hundred per cent (100%) of the amount of issued ordinary shares, a General Meeting of Shareholders shall be convened and held within four weeks of the issue in which the reasons for the issue shall be explained.

7.7

The provisions of paragraphs 1 through 5 of this Article 7 shall be equally applicable to the granting of rights to subscribe for shares but shall not be applicable to the issue of shares to Persons exercising a previously granted right to subscribe for shares.

7.8

In the event of an issue of preference shares, a General Meeting of Shareholders shall be convened, to be held not later than two years after the date on which preference shares were issued for the first time. The agenda for that meeting shall include a resolution relating to the repurchase or cancellation of the preference shares. If the resolution to be adopted in respect of this item on the agenda is not directed to the repurchase or cancellation of the preference shares, a General Meeting of Shareholders shall be convened and held, in each case within two years of the previous meeting, the agenda of these meetings shall include a resolution relating to the repurchase or cancellation of the preference shares, until such time as no more preference shares shall be issued. The foregoing provisions of this paragraph 8 do not apply to preference shares issued pursuant to a resolution or with concurrence of the General Meeting.

7.9

Section 2:96 of the Dutch Civil Code also applies to the issuance of shares and the granting of rights to subscribe for shares.

Article 8. Conditions of Issuance; Rights of Pre-emption.

- 8.1 The price and further conditions of issuance shall be determined in the resolution to issue shares. The issue price of may be no lower than par value, without prejudice to the provision of Section 2:80, subsection 2, of the Dutch Civil Code.
- 8.2 Upon the issuance of ordinary shares, every holder of ordinary shares shall have a right of pre-emption in accordance with Section 2:96a of the Dutch Civil Code. The same applies to the granting of rights to subscribe for ordinary shares.
- 8.3 The rights of pre-emption may be restricted or excluded by a resolution of the Board of Management. The resolution shall be subject to the approval of the Supervisory Board. The authority granted to the Board of Management shall terminate on the date of termination of the authority of the Board of Management to issue shares. Article 7, paragraphs 1 through 4, of these Articles of Association, shall apply by analogy.
- 8.4 Furthermore, the conditions of issuance and rights of pre-emption shall be subject to the provisions of Sections 2:96a and 2:97 of the Dutch Civil Code.

Article 9. Payment for Shares.

- 9.1 Upon the issuance of an ordinary share, the nominal value of the share issued must be paid together with, if the share is taken up at a price higher than par value, the difference between these amounts, without prejudice to the provisions in Section 2:80, subsection 2, of the Dutch Civil Code. Upon the issuance of a preference share, at least one fourth of the par value shall be paid. Further payments on preference shares shall be made, up to the nominal value as a maximum, at the request of the Board of Management, approved by the Supervisory Board.
- 9.2 Payment for ordinary shares must be made in cash to the extent that no other manner of payment has been agreed upon. Payment for preference shares can only be made in cash.
- 9.3 The Board of Management shall be authorised to enter into transactions concerning non-monetary contributions on ordinary shares, and the other transactions referred to in Section 2:94, subsection 1, of the Dutch Civil Code, without the prior approval of the General Meeting. The resolution to enter into these transactions shall require the approval of the Supervisory Board.
- 9.4 Payments on shares and non-cash contribution shall furthermore be subject to Sections 2:80, 2:80a, 2:80b and 2:94b of the Dutch Civil Code.

CHAPTER V. OWN SHARES AND DEPOSITARY RECEIPTS.

Article 10.

- 10.1 The Company shall be entitled to acquire fully paid-up shares in its own capital or depositary receipts, provided either no valuable consideration is given or provided that:
- (a) the distributable part of the capital and reserves is at least equal to the purchase price; and
 - (b) the nominal value of the shares or the depositary receipts thereof which the Company acquires, holds or holds in pledge or which are held by a Subsidiary does not exceed one tenth of the Company's issued capital.
- 10.2 The Board of Management shall require the authorisation of the General Meeting for an acquisition for valuable consideration. This authorisation may be given for a maximum of eighteen months. At the time of granting such authorisation, the General Meeting must determine how many shares or depositary receipts thereof may be acquired and between which limits the price must be.

10.3 The Company may acquire its own shares or depositary receipts thereof in order to transfer them, pursuant to a regulation to that effect, to staff employed by the Company or by a Group Company.

10.4 The acquisition or alienation by the Company of its own shares shall take place pursuant to a decision of the Board of Management. Such a decision shall be subject to the approval of the Supervisory Board, without prejudice to the provisions of paragraph 2 of this Article 10.

10.5 Own shares and depositary receipts thereof shall furthermore be subject to Sections 2:89a, 2:95, 2:98, 2:98a, 2:98b, 2:98c, 2:98d and 2:118 of the Dutch Civil Code.

CHAPTER VI. REDUCTION OF THE COMPANY'S ISSUED CAPITAL.

Article 11.

11.1 The General Meeting may decide to reduce the Company's issued capital, but only at the proposal of the Board of Management with the approval of the Supervisory Board:

- (a) by cancelling shares; or
- (b) by reducing the nominal value of shares by amending these Articles of Association.

A resolution of the General Meeting to reduce the Company's issued capital must specify the shares to which the resolution relates and must include provisions for the implementation of the resolution.

11.2 A resolution to cancel shares may only involve:

- (a) shares or depositary receipts thereof held by the Company itself or the depositary receipts of which (if any) are held by the Company itself; or
- (b) all shares of one particular class, in each case with the consent of the meeting of holders of shares of the class concerned and with repayment.

11.3 In the event of cancellation of all preference shares, without prejudice to any provision of the law on the subject, there shall, to the extent possible, be paid in respect of these shares an amount equal to the nominal value paid on those shares, increased by any outstanding dividend referred to in Article 31, paragraph 1, of these Articles of Association which dividend shall then be calculated over the period ending on the date on which the payment shall become payable.

11.4 Partial repayment of shares or exemption from the obligation to pay calls on shares is only possible in order to implement a resolution to reduce the nominal value of the shares. Such repayment or exemption shall take place:

- (a) with regard to all shares; or
- (b) with regard to all shares of one particular class, in each case with the consent of the meeting of holders of shares of the class concerned.

CHAPTER VII. TRANSFER OF SHARES.

Article 12.

12.1 The transfer of a registered share or the transfer of a right in rem therein shall be effected by means of a deed and, except where the Company itself is a party to the transaction, acknowledgement in writing of the transfer by the Company.

Acknowledgement is effected in the deed, or by a dated declaration of acknowledgement either on the deed or on a copy or extract thereof which is certified by a civil law notary or by the

transferor. Official service of that deed or that copy or extract on the Company shall rank as acknowledgement.

12.2

A right of pledge may also be created without acknowledgement or official service of notice to the Company. In such case, Section 3:239 of the Dutch Civil Code shall apply by analogy, on the understanding that the communication referred to in subsection 3 of that Section, shall then be replaced by acknowledgement by or official service on the Company.

12.3

A member of the Board of Management shall sign the acknowledgement or another Person authorised to do so by the Board of Management.

12.4

The provisions of paragraphs 1 and 3 of this Article 12 shall apply by analogy to the allocation of registered shares on the division of jointly held property.

12.5

The Shareholder shall have voting rights in respect of a share in which the life interest or the right of pledge is created. However, the voting rights shall accrue to the beneficiary of the life interest or the pledgee in the event that it was so stipulated at the creation of the life interest or the right of pledge. The Shareholder who holds no voting rights and the beneficiary of a life interest or pledgee who does hold voting rights shall have the rights which the law attributes to holders of depositary receipts issued for shares in a company which are issued with that company's co-operation. A beneficiary of a life interest or a pledgee who holds no voting rights shall not have the rights referred to in the preceding sentence.

12.6

The rights deriving from a share in which a life interest is created, relating to the acquisition of shares shall accrue to the Shareholder. However, the Shareholder shall compensate the beneficiary of the life interest for the value thereof to the extent that the latter is entitled thereto by virtue of his life interest.

12.7

A priority share can be freely transferred to the Company.

12.8

Except as provided in paragraph 7, the transfer of a priority share can only be effected with the approval of both the Board of Management and the Supervisory Board. In that case, the transfer must take place within three months after the approval has been granted. The approval shall be deemed to have been granted if the Board of Management and the Supervisory Board, having informed the applicant of the refusal of the request, do not simultaneously inform the applicant of one or more prospective buyers who are prepared to purchase the priority share concerned against payment in cash. The Company itself can be designated as a prospective buyer.

12.9

The transfer of a priority share to the Company or to another prospective buyer as referred to in paragraph 8 shall take place against a purchase price that equals the nominal value of such priority share.

CHAPTER VIII. THE BOARD OF MANAGEMENT.

Article 13. The Board of Management.

13.1

The management of the Company shall be constituted by the Board of Management.

13.2

The Supervisory Board shall determine the number of members of the Board of Management after consultation with the Chief Executive Officer.

Article 14. Appointment.

14.1

Members of the Board of Management shall be appointed by the General Meeting from a list of candidates to be drawn up by the Supervisory Board.

- 14.2 If the list of candidates contains the names of at least two Persons it shall be binding. 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.
- 14.3 If the Supervisory Board should fail to draw up a list of nominees within three months after the vacancy has occurred the General Meeting may appoint a member of the Board of Management at its own discretion.
- 14.4 If the Supervisory Board has drawn up a non-binding nomination, the appointment of a Person to the Board of Management in contravention of the nomination shall require a resolution of the General Meeting adopted with an absolute majority of the votes cast representing more than one third of the Company's issued capital.
- 14.5 The Supervisory Board shall appoint a member of the Board of Management as "Chief Executive Officer".

Article 15. Suspension and Removal.

- 15.1 Each member of the Board of Management may be suspended or removed by the General Meeting at any time.
- 15.2 A resolution to suspend, remove or revoke the suspension of a member of the Board of Management 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 more than one third of the Company's issued capital.
- 15.3 The Supervisory Board can suspend each member of the Board of Management at any time. The General Meeting may discontinue a suspension by the Supervisory Board at any time.
- 15.4 Any suspension may be extended one or more times, but may not last longer than three months in the aggregate. If at the end of that period no decision has been taken on termination of the suspension, or on removal, the suspension shall cease.
- 15.5 Each member of the Board of Management shall retire not later than the day on which the first AGM is held after four years have elapsed from his appointment. Each resigning member of the Board of Management may be re-appointed.

Article 16. Remuneration.

The Supervisory Board shall determine the remuneration of the individual members of the Board of Management, on a proposal by the Remuneration Committee, within the scope of the remuneration policy adopted by the General Meeting.

Article 17. Duties of the Board of Management; Decision-making Process; Allocation of Duties.

- 17.1 Subject to the restrictions imposed by these Articles of Association, the Board of Management shall be entrusted with the management of the Company.
- 17.2 The Board of Management shall draw up a set of rules governing its internal functioning and the passing of resolutions by the Board of Management (the "**By-laws Board of Management**"). The adoption, amendment, modification, replacement or suspension of the By-Laws Board of Management shall require the approval of the Supervisory Board.
- 17.3 All decisions of the Board of Management shall be adopted by an absolute majority of the votes cast, unless otherwise provided in the By-Laws Board of Management.

17.4 The Board of Management may determine the duties with which each member of the Board of Management will be charged in particular. The allocation of duties shall require the approval of the Supervisory Board.

17.5 The Board of Management shall, whether or not from among its members, appoint "Officers" and allocate certain of its duties to these Officers including a general or limited power of attorney to represent the Company. This allocation shall not effect the ultimate responsibility of the Board of Management for the duties thus allocated. The appointment and removal of Officers shall require the approval of the Supervisory Board.

17.6 The Board of Management shall appoint a "**Company Secretary**" who will assist the Board of Management. The appointment and removal of the Company Secretary shall require the approval of the Supervisory Board.

Article 18. Representation of the Company.

18.1 The Board of Management shall be authorised to represent the Company. Each member of the Board of Management shall also be authorised to represent the Company.

18.2 In the event of a conflict of interest between the Company and a member of the Board of Management, the Company shall be represented by the Person or Persons designated for such purpose by the Supervisory Board, save when one or more other Persons have been designated by the General Meeting.

Article 19. Approval of Resolutions of the Board of Management.

19.1 Without prejudice to any other provision of these Articles of Association, the Board of Management shall require approval of the Supervisory Board for managerial resolutions with respect to:

- a. all transactions between the Company and natural or legal persons who hold at least ten percent (10%) of the shares in the Company that are of material significance to the Company and/or such persons;
- b. 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;
- c. all transactions in which there are conflicts of interest with members of the Board of Management that are of material significance to the Company and/or the relevant members of the Board of Management;
- d. 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;
- e. 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;
- f. participating, or otherwise taking an interest in or acceptance or disposal of the management of other business enterprises and terminating or modifying such participation or interest;
- g. entering into, terminating and amending joint venture and pooling agreements;
- h. acquiring fixed business assets for an amount as determined by the Supervisory Board and notified to the Board of Management, each acquisition to be considered separately; and
- i. 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.

19.2

The Supervisory Board may determine that a resolution as referred to in paragraph 1, shall not require its approval if the amount involved does not exceed a value fixed by the Supervisory Board and notified to the Board of Management in writing.

19.3

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. Such resolutions shall be clearly specified and notified to the Board of Management in writing.

19.4

The lack of approval of the Supervisory Board in respect of a resolution referred to in this Article 19 does not affect the authority of the Board of Management or its members to represent the Company.

Article 20. Vacancy or Inability to Act.

20.1

If a seat is vacant on the Board of Management (*'ontstentenis'*) or a member of the Board of Management is unable to perform his duties (*'belet'*), the remaining members or member of the Board of Management shall be temporarily entrusted with the entire management of the Company. If all seats in the Board of Management are vacant or all members or the sole member of the Board of Management, as the case may be, are unable to perform their duties, the management of the Company shall be temporarily entrusted to the Supervisory Board which shall then be authorised to temporarily entrust the management to one or more Persons, whether or not from among its members.

20.2

The Supervisory Director who is temporarily entrusted with the management of the Company, when all seats in the Board of Management are vacant or all members or the sole member of the Board of Management, as the case may be, are unable to perform their duties, shall resign from the Supervisory Board.

Article 21. Management Committee.

21.1

The Company has a Management Committee, consisting of a number of members to be determined by the Board of Management. The Company Secretary shall be a member of the Management Committee.

21.2

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

21.3

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

21.4

The Board of Management may establish terms of reference for the Management Committee (the "**Terms of Reference for the Management Committee**"). The adoption, amendment, modification, replacement or suspension of the Terms of Reference for the Management Committee shall require the approval of the Supervisory Board.

CHAPTER IX. THE SUPERVISORY BOARD.

Article 22. Number of Supervisory Directors.

22.1 The Company shall have a Supervisory Board consisting of Supervisory Directors. Individuals only can be Supervisory Directors.

22.2 The Supervisory Board shall have at least three Supervisory Directors. Subject to this minimum, the Supervisory Board shall determine the number of Supervisory Directors after consultation with the Chief Executive Officer.

22.3 If less than three Supervisory Directors are in office, the Supervisory Board shall still be validly constituted, but shall proceed without delay to make up its number.

Article 23. Appointment.

23.1 The Supervisory Directors shall be appointed by the General Meeting from a list of candidates to be drawn up by the Priority.

23.2 The provisions of Article 14, paragraphs 2, 3 and 4, of these Articles of Association shall apply by analogy to the appointment of Supervisory Directors.

23.3 A nomination or recommendation to the General Meeting of Shareholders to appoint a Supervisory Director shall state the candidate's age, his profession, the amount of the shares he holds in the Company's capital and the positions he holds or has held, insofar as these are relevant for the performance of the duties of a Supervisory Director. Furthermore, the legal entities of whose supervisory boards he is also a member of must be listed; if those include legal entities which belong to the same group, reference to that group is sufficient. The recommendation or nomination for appointment or reappointment shall state the reasons on which it is based.

Article 24. Suspension and Removal; Retirement.

24.1 Each Supervisory Director may be suspended or removed by the General Meeting at any time.

24.2 The provisions of Article 15, paragraphs 2 and 4, of these Articles of Association shall apply by analogy to the suspension, removal and the revocation of suspension of Supervisory Directors, except that the proposal should be made by the Priority.

24.3 Each Supervisory Director shall retire not later than the day on which the first AGM is held after four years have elapsed from his appointment. Each resigning Supervisory Director may be re-appointed, provided that a person may be appointed to the Supervisory Board for a maximum of three (3) four-year terms.

24.4

The Supervisory Directors shall retire periodically in accordance with a rotation plan to be drawn up by the Supervisory Board.

Article 25. Remuneration.

The General Meeting shall determine the remuneration for every member of the Supervisory Board.

Article 26. Duties and Powers.

26.1

It shall be the duty of the Supervisory Board to supervise the Board of Management's management and the general course of affairs in the Company and in the business connected with it. The Supervisory Board shall advise the Board of Management. In performing their duties the Supervisory Directors shall act in accordance with the interests of the Company and of the business connected with it.

26.2

The Board of Management shall promptly supply the Supervisory Board with the information required for the performance of its duties.

26.3

Each Supervisory Director shall have access to the buildings and premises of the Company and shall be authorised to inspect the books and records of the Company in so far as required or as is useful for the proper performance of his duties. The Supervisory Board may be assisted by experts in exercising its duties.

26.4

The Supervisory Board may appoint from amongst its members a "**delegated Supervisory Director**" (*'gedelegeerd commissaris'*). A delegated Supervisory Director is a Supervisory Director who has a special duty. The delegation may not extend beyond the duties of the Supervisory Board itself and may not include the management of the Company. It may entail more intensive supervision and advice and more regular consultation with the Board of Management. The delegation shall be of a temporary nature only. The delegation may not detract from the role and power of the Supervisory Board. The delegated Supervisory Director remains a member of the Supervisory Board.

26.5

The Supervisory Board may appoint standing and/or ad hoc committees from among its members, which are charged with tasks specified by the Supervisory Board. The composition of any committee is determined by the Supervisory Board. The Supervisory Board shall, in any event, establish an "**Audit Committee**", a "**Remuneration Committee**" and a "**Nomination Committee**".

Article 27. Proceedings and Decision-making Process.

27.1

With due observance of the provisions of these Articles of Association, the Supervisory Board shall adopt a set of regulations concerning the division of duties within the Supervisory Board and its internal procedures (the "**By-laws Supervisory Board**").

27.2

The Supervisory Board shall elect a Chairman and a Vice-Chairman from among its members. The Vice-Chairman replaces, and assumes the powers and duties of, the Chairman in the latter's absence. The Chairman shall not be a former member of the Board of Management.

27.3

The Chairman is primarily responsible for the functioning of the Supervisory Board and its committees. He shall act as the spokesman of the Supervisory Board and is the main contact for the Chief Executive Officer and the Board of Management as a whole. The Chief Executive Officer and the Chairman of the Supervisory Board shall meet on a regular basis.

27.4

The Supervisory Board is assisted by the Company Secretary, who is appointed in accordance with the provisions of Article 17, paragraph 6.

- 27.5 The Company Secretary or any other person designated for such purpose by the chairman of a meeting of the Supervisory Board shall draw up a report on the proceedings at the meeting. The report should provide insight into the decision-making process at the meeting. The report shall be adopted by the Supervisory Board at the same meeting, or the next meeting.
- 27.6 All decisions of the Supervisory Board shall be adopted by an absolute majority of the votes cast unless otherwise provided for in these Articles of Association or the By-laws Supervisory Board.
- 27.7 Except as provided in paragraph 9 of this Article 27 or the By-laws Supervisory Board, decisions of the Supervisory Board shall only be valid if taken at a meeting at which the majority of the Supervisory Directors are present or represented.
- 27.8 A co-member of the Supervisory Board authorised in writing may represent a Supervisory Director. The expression "in writing" shall include any message transmitted by current means of communication and received in writing. A Supervisory Director may not act as representative for more than one co-member.
- 27.9 Supervisory Board resolutions may also be adopted in writing, provided the proposal concerned is submitted to all Supervisory Directors then in office and none of them objects to this form of adoption. Adoption of resolutions in writing shall be effected by statements in writing from all the Supervisory Directors. A statement from a Supervisory Director who wishes to abstain from voting on a particular resolution which is adopted in writing must reflect the fact that he does not object to this form of adoption.
- 27.10 A resolution adopted by the Supervisory Board may be evidenced outside the Company through a statement from the Chairman and/or the Company Secretary.
- 27.11 The Supervisory Board shall meet together with the Board of Management as often as the Supervisory Board or the Board of Management deems such necessary.

Article 28. Indemnification; Limited liability.

- 28.1 The Company shall indemnify any Person who is or was a Supervisory Director or a member of the Board of Management and who was or is a party or is threatened to be made a party to any threatened, pending or completed action, suit or proceeding, whether civil, criminal, administrative or investigative (other than an action by or in the right of the Company) by reason of the fact that he is or was a Supervisory Director, member of the Board of Management, Officer, employee or agent of the Company, or is or was serving at the request of the Company as a supervisory director, member of the management board, officer, director, employee, trustee or agent of another company, a partnership, joint venture, trust or other enterprise or entity, including with respect to employee benefit plans maintained or sponsored by the Company or for the benefit of its or any of its group companies' employees or consultants. This indemnification is applicable to all expenses (including attorneys' fees), judgements, fines and amounts paid in settlement actually and reasonably incurred by such Person in connection with such action, suit or proceeding if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company, and, with respect to any criminal action or proceeding, had no reasonable cause to believe his conduct was unlawful or outside of his mandate. The termination of any action, suit or proceeding by a judgement, order, settlement, conviction, or upon a plea of nolo contendere or its equivalent, shall not, of itself, create a presumption that the Person did not act in good faith and not in a manner which he reasonably could believe to be in or not opposed to the best interests of the Company, and, with respect to any criminal action or proceeding, had reasonable cause to believe that his conduct was unlawful.
- 28.2 The Company shall indemnify any Person who is or was a Supervisory Director or a member of the Board of Management and who was or is a party or is threatened to be made a party to any

threatened, pending or completed action or proceeding by or in the right of the Company to procure a judgement in its favour, by reason of the fact that he is or was a Supervisory Director, member of the Board of Management, Officer, employee or agent of the Company, or is or was serving at the request of the Company as a supervisory director, member of the management board, officer, director, employee, trustee or agent of another company, a partnership, joint venture, trust or other enterprise or entity, including with respect to employee benefit plans maintained or sponsored by the Company or for the benefit of its or any of its group companies' employees or consultants. This indemnification is applicable to all expenses (including attorneys' fees) judgements, fines and amounts paid in settlement, actually and reasonably incurred by him in connection with such action, suit or proceeding if he acted in good faith and in a manner he reasonably believed to be in or not opposed to the best interests of the Company, except that no indemnification shall be made in respect of any claim, issue or matter as to which such Person shall have been adjudged to be liable for gross negligence or wilful misconduct in the performance of his duty to the Company, unless and only to the extent that the court in which such action or proceeding was brought or any other court having appropriate jurisdiction shall determine upon application that, despite the adjudication of liability but in view of all of the circumstances of the case, such Person is fairly and reasonably entitled to indemnification against such expenses which the court in which such action or proceeding was brought or such other court having appropriate jurisdiction shall deem proper.

28.3

To the extent that a Supervisory Director or member of the Board of Management, Officer, employee or agent of the Company has been successful on the merits or otherwise in defence of any action, suits of proceeding, referred to in paragraphs 1 and 2, or in defence of any claim, issue or matter therein, he shall be indemnified against all expenses (including attorneys' fees) actually and reasonably incurred by him in connection therewith.

28.4

Any indemnification by the Company referred to in paragraphs 1 and 2 shall (unless ordered by a court) only be made by the Company upon a determination that indemnification of the Supervisory Director or member of the Board of Management is proper under the circumstances because he had met the applicable standard of conduct set forth in paragraph 1 and 2 of this article 28. Such determination shall be made:

a.

by a decision of the Supervisory Board adopted by a majority of the votes cast by Supervisory Directors who are not parties to such action, suit or proceeding, even though such decision is taken at a meeting at which such Supervisory Directors present or represented are less than a majority of all the Supervisory Directors, or;

b.

if there are no Supervisory Directors who are not named as parties to such action, suit or proceeding or if the Supervisory Directors who are not named as parties to such action, suit or proceeding so direct, by independent legal counsel in a written opinion; or

c.

by the General Meeting.

28.5

Expenses (including attorney's fees) incurred by a Supervisory Director or a member of the Board of Management in defending a civil or criminal action, suit or proceeding may be paid by the Company in advance of the final disposition of such action, suit or proceeding upon receipt of an undertaking by or on behalf of the Supervisory Director or member of the Board of Management to repay such amount if it shall ultimately be determined that he is not entitled to be indemnified by the Company as authorised in this article. Such expenses incurred by Officers, employees or agents may be so paid upon such terms and conditions as the Supervisory Board decides.

28.6

The indemnification provided for by this article shall not be deemed exclusive of any other right to which a Person seeking indemnification or advancement of expenses may be entitled under the laws of the Netherlands as from time to time amended or under any by-laws, agreement, resolution

of General Meeting or of the disinterested members of the Supervisory Board or otherwise, both as to actions in his official capacity and as to actions in another capacity while holding such position, and shall continue as to a Person who has ceased to be a Supervisory Director, member of the Board of Management, Officer, director, employee, trustee or agent and shall also inure to the benefit of the heirs, executors, administrators and the estate of such a Person. The Company may, to the extent authorised from time to time by the Supervisory Board, grant rights to indemnification and to the advancement of expenses to any officer, employee or agent of the Company to the fullest extent of the provisions of this Article 28 with respect to the indemnification and advancement of expenses of Supervisory Directors and members of the Board of Management of the Company.

28.7

The Company may, to the extent authorised from time to time by the Supervisory Board, purchase and maintain insurance on behalf of any Person who is or was a Supervisory Director, member of the Board of Management, Officer, employee or agent of the Company, or is or was serving at the request of the Company as a supervisory director, member of the management board, officer, director, employee, trustee or agent of another company, a partnership, joint venture, trust or other enterprise, or entity, against any liability asserted against him and incurred by him in any such capacity or arising out of his capacity as such, whether or not the Company would have the power to indemnify him against such liability under the provisions of this Article.

28.8

Whenever in this article reference is made to the Company, this shall include, in addition to the resulting or surviving company also any constituent company (including any constituent company of a constituent company) absorbed in a consolidation or merger which, if its separate existence had continued, would have had the power to indemnify its supervisory directors, members of the management board, officers, employees and agents, so that any Person who is or was a supervisory director, member of the management board, officer, employee or agent of such constituent company, or is or was serving at the request of such constituent company as a supervisory director, member of the management board, officer, director, employee, trustee or agent of another company, a partnership, joint venture, trust or other enterprise or entity, shall stand in the same position under the provisions of this article with respect to the resulting or surviving company as he would have with respect to such constituent company if its separate existence had continued.

No Person shall be personally liable to the Company or its shareholders for monetary damages for breach of fiduciary duty as a Supervisory Director or member of the Board of Management; provided, however, that the foregoing shall not eliminate or limit the liability of a Supervisory Director or member of the Board of Management (1) for any breach of such individual's duty of loyalty to the Company or its shareholders, (2) for acts or omissions not in good faith or which involve intentional misconduct or a knowing violation of law, (3) for any transaction from which the director derived an improper personal benefit or (4) for personal liability which is imposed by Dutch law, as from time to time amended. No amendment, repeal or modification of this Article 28 shall adversely affect any right or protection of any Person entitled to indemnification or advancement of expenses under this Article 28 prior to such amendment, repeal or modification.

CHAPTER X. ANNUAL ACCOUNTS AND ANNUAL REPORT; DISTRIBUTIONS.

Article 29. Financial Year; Annual Accounts and Annual Report.

29.1

The Company's financial year shall be the calendar year.

29.2

Annually, the Board of Management shall prepare annual accounts and shall deposit these at the Company's office for inspection by Shareholders, not later than five months after the end of the financial year, unless by reason of special circumstances this period is extended by the General Meeting by not more than six months. Within this period, the Board of Management shall also deposit the annual report for inspection by the Shareholders.

- 29.3 Within the period referred to in paragraph 2, the Board of Management shall also submit the annual accounts and the annual report to the Supervisory Board.
- 29.4 The Supervisory Board shall present its report on the annual accounts to the General Meeting.
- 29.5 The annual accounts and the annual report shall furthermore be subject to Sections 2:101, 2:102 and 2:103 and Title 9, Book 2 of the Dutch Civil Code.

Article 30. Adoption of the Annual Accounts and Release from Liability.

- 30.1 The General Meeting shall adopt the annual accounts.
- 30.2 After adoption of the annual accounts, the General Meeting shall pass a resolution concerning release of the members of the Board of Management and the Supervisory Directors from liability for the exercise of their respective duties, insofar as the exercise of such duties is reflected in the annual accounts or otherwise disclosed to the General Meeting prior to the adoption of the annual accounts. The scope of a release from liability shall be subject to limitations by virtue of the law.

Article 31. Profits; Dividends.

- 31.1 Annually, out of the profits—the positive balance of the profit and loss account—an amount of dividend shall be paid on the preference shares of which the percentage—to be calculated over the paid up part of the nominal value—is equal to the average deposit rate of the European Central Bank, decreased or increased by a discount or upcount, with a maximum of three percent (3%), to be determined by the Board of Management under the approval of the Supervisory Board at the occasion of the first issue of a preference share, averaged over the number of days over which the payment is made. If for any financial year the distribution referred to above cannot or cannot entirely be made because the profit does not so allow, payment of deficit shall be made from the profit of one or more of the following financial years. Subsequently on the priority share a dividend equal to five percent (5%) of their nominal value shall be paid.
- 31.2 Subsequently, the Board of Management shall, subject to the approval of the Supervisory Board, determine which part of the profit remaining after application of paragraph 1 shall be allocated to the reserves.
- 31.3 Any part of the profits remaining thereafter shall be paid as a dividend on the ordinary shares.
- 31.4 Distributions may be made only up to an amount that does not exceed the amount of the Distributable Equity.
- 31.5 The Board of Management, with the approval of the Supervisory Board, may resolve to make interim distributions.
- 31.6 In addition, distributions to Shareholders are subject to Sections 2:103, 2:104 and 2:105 of the Dutch Civil Code.
- 31.7 All distributions on ordinary shares, either as an (interim)dividend or otherwise, shall be made such that on each ordinary share an equal amount or value shall be paid.

Article 32. Distribution in Shares or Other Securities and Distributions at the Charge of Reserves.

- 32.1 The General Meeting may, at the proposal of the Board of Management which has been approved by the Supervisory Board, resolve that a payment of dividend on ordinary shares be wholly or partly paid by a distribution of shares or any other securities in the Company or any other Person.
- 32.2 In contravention of the provision in paragraph 1, a resolution to make an (interim) distribution on ordinary shares in shares in the Company (or any securities in the Company that are convertible

into, exercisable or exchangeable for, or evidence the right to purchase any shares) may be adopted by the Board of Management, subject to approval of the Supervisory Board, if at such time the Board of Management is authorised in accordance with Article 7 of these Articles of Association to issue the shares (or other aforementioned securities in the Company) concerned.

32.3

The General Meeting may, at the proposal of the Board of Management which has been approved by the Supervisory Board, resolve that distributions to Shareholders be made at the charge of one or more of the Company's reserves. Paragraph 1 shall apply by analogy.

32.4

The Board of Management, subject to approval of the Supervisory Board, may decide to effect payment of the amounts payable to holders of preference shares in accordance with Article 31, paragraph 1, of these Articles of Association by such payment being charged to one or more of the Company's reserves.

Article 33. Date for Payment.

Dividends and other distributions shall be made payable on the date to be determined by the Board of Management. The making payable shall be announced in accordance with Article 43 of these Articles of Association.

CHAPTER XI. GENERAL MEETINGS OF SHAREHOLDERS.

Article 34. The AGM.

34.1

The AGM shall be held annually, within six months of the end of the financial year.

34.2

The agenda for the AGM shall contain, inter alia, the following matters:

- (a) the annual report;
- (b) corporate governance;
- (c) reservation and dividend policy;
- (d) adoption of the annual accounts;
- (e) release from liability of the members of the Board of Management and the Supervisory Directors;
- (f) appointments to any vacancies;
- (g) any other proposals put forward for discussion by the Supervisory Board or the Board of Management, such as proposals concerning the designation of a company body competent to issue shares and to grant rights to subscribe for shares and the authorisation of the Board of Management to cause the Company to acquire own shares or depository receipts thereof.

Article 35. Other General Meetings of Shareholders.

Other General Meetings of Shareholders shall be held as often as the Supervisory Board or the Board of Management deems such necessary, without prejudice to the provisions of Sections 2:110, 2:111 and 2:112 of the Dutch Civil Code.

Article 36. Notice; Agenda.

36.1

The Supervisory Board or the Board of Management shall convene the General Meetings of Shareholders.

36.2

Notice of the meeting shall be given no later than on the fifteenth day prior to the date of the meeting.

- 36.3 The notice of the meeting shall state the subjects to be dealt with or it shall state that the Shareholders may find details thereof at the Company's office, without prejudice to the provisions of Article 44, paragraph 2, of these Articles of Association and of Section 2:99, subsection 7, of the Dutch Civil Code.
- 36.4 The notice of the meeting shall state the requirement for admission to the meeting as described in Article 40 of these Articles of Association.
- 36.5 Notice shall be given in the manner stated in Article 43 of these Articles of Association.
- 36.6 Matters not stated in the notice of the meeting may be further announced, subject to the time limit pertaining to the convocation of meetings, in the manner stated in Article 43 of these Articles of Association.
- 36.7 Unless the notice of the meeting includes the contents of all documents which, according to the law or these Articles of Association, are to be available to Shareholders for inspection in connection with the meeting to be held, these documents are to be made available free of charge to Shareholders in Amsterdam at the office of a paying agent (*'betaalkantoor'*) as referred to in the Euronext Listing Rules.
- 36.8 Shareholders representing alone, or in the aggregate, at least one percent (1%) of the Company's issued capital or—according to the Euronext Official Price List—at least a value of fifty million euro (EUR 50,000,000), have the right to request the Board of Management or the Supervisory Board to place items on the agenda of the General Meeting of Shareholders.

These requests shall in principal be honoured by the Board of Management or the Supervisory Board on the condition:

- a. that the Shareholders have a reasonable interest in the items to be considered;
- b. that the placing on the agenda is not in conflict with an orderly course of the meeting and that there shall be no grave interests of the Company which resist against the placing on the agenda;
- c. that the request has been filed in writing with the Board of Management or the Chairman of the Supervisory Board at least sixty (60) days prior to the date of the General Meeting of Shareholders.

- 36.9 Where used in this Article 36, the term "Shareholders" shall include beneficiaries of a life interest and pledgees to whom the voting rights on shares accrue.

Article 37. Venue of Meetings.

The General Meetings of Shareholders shall be held in Leiden, Amsterdam, Haarlemmermeer (including but not limited to Schiphol Airport and Schiphol-Rijk), Utrecht, Rotterdam or The Hague.

Article 38. Chairmanship.

- 38.1 The General Meetings of Shareholders shall be chaired by the Chairman of the Supervisory Board or, in his absence, by the Vice Chairman of that board; in the event that the latter is also absent, the Supervisory Directors present shall elect a chairman from their midst. The Supervisory Board may designate another Person to act as chairman of a General Meeting of Shareholders.
- 38.2 If the chairman of the meeting has not been appointed in accordance with paragraph 1, the meeting shall itself choose a chairman. Until the time such choice is made a member of the Board of Management designated thereto by the Board of Management shall act as chairman.

Article 39. Minutes.

39.1 A secretary to be designated by the chairman of the meeting shall keep minutes of the proceedings at every General Meeting of Shareholders.

39.2 The minutes of a General Meeting of Shareholders shall be made available, on request to Shareholders no later than three months after that General Meeting of Shareholders, after which the Shareholders shall have the opportunity to react to the minutes in the following three months. The minutes are then adopted by the chairman and the secretary of the meeting and shall be signed by them as evidence thereof.

39.3 The Supervisory Board or the chairman of the meeting may determine that notarial minutes shall be drawn up of the proceedings of the meeting, in which case the provisions of this Article 39 may be disregarded. The notarial minutes shall be co-signed by the chairman.

Article 40. Rights at Meetings; Admittance.

40.1 Each Shareholder entitled to vote and each beneficiary of a life interest or pledgee to whom the voting rights accrue shall be entitled to attend the General Meeting of Shareholders, to address the meeting and to exercise his voting rights. Where it concerns registered shares, the Board of Management must be notified in writing of the intention to attend the meeting. The Board of Management must receive such notice not later than on the date mentioned in the notice of the meeting.

40.2 The right to take part in the meeting in accordance with paragraph 1 may be exercised by a proxy authorised in writing, provided that the power of attorney has been received by the Board of Management not later than on the date mentioned in the notice of the meeting.

40.3 The date mentioned in the notice of the meeting, referred to in paragraphs 1 and 2, shall not be earlier than the seventh day prior to the date of the meeting.

40.4 If the voting rights attributable to a share accrue to the beneficiary of a life interest or to a pledgee, instead of to the Shareholder, the Shareholder is also authorised to attend the General Meeting of Shareholders and to address the meeting, provided that, where it concerns registered shares, the Board of Management has been notified of the intention to attend the meeting in accordance with paragraph 1. Paragraph 2 of this Article 40 shall apply by analogy.

40.5 With respect to the voting rights and/or the right to participate in meetings the Company shall on the basis of the provisions of Sections 2:88 and 2:89 of the Dutch Civil Code also recognise as Shareholder the Person mentioned in a written statement of a Necigef-participant as a Necigef-beneficiary, entitled to a given number of bearer shares belonging to such Necigef-participant's collective deposit of shares in the Company, provided that in the statement it is also confirmed that the Necigef-beneficiary shall remain thus entitled until the close of the meeting and provided further that the statement is filed in time at such place as stated in the notice of the meeting, against a receipt, which receipt shall serve as a ticket of admission for the meeting. The date on which the filing of the statement must have been effected at the latest shall be specified in the notice of the meeting. This date shall not be earlier than the seventh day prior to the date of the meeting.

40.6 If the Board of Management so decides, a record date shall be scheduled for a General Meeting of Shareholders. This record date shall not be earlier than the seventh day prior to the date of the meeting. If this record date is scheduled the voting rights and the right to attend the meeting shall accrue to those holding such entitlements, and registered as such in a register designated for that purpose by the Board of Management, on this record date, irrespective of to whom these rights accrue at the time of the General Meeting of Shareholders.

The record date scheduled shall be specified in the notice of the meeting together with the manner in which Persons with voting rights and the right to attend the meeting can register and exercise their rights.

The provisions of paragraphs 1, 2, 4 and 5 shall apply accordingly, provided that the written statements addressed to the Board of Management can be made by the keeper of the register referred to in this paragraph 6 and with respect to bearer shares that the statement does not need to confirm that the Person mentioned therein shall remain a Necigef-beneficiary until the close of the meeting.

- 40.7 Each share confers the right to cast one (1) vote.
- 40.8 Each Person entitled to vote or his proxy shall sign the attendance list.
- 40.9 The Supervisory Directors and the members of the Board of Management shall, as such, have the right to advise the General Meeting of Shareholders.
- 40.10 The chairman of the meeting shall decide whether Persons other than those who shall be admitted in accordance with the above provisions of this article shall be admitted to the meeting.

Article 41. Adoption of Resolutions and Voting.

- 41.1 Valid resolutions of the General Meeting can only be adopted in a General Meeting of Shareholders for which notice is given and which is held in accordance with the relevant provisions of the law and of these Articles of Association. Except where the law or these Articles of Association require a qualified majority, the absolute majority of the votes cast shall adopt all resolutions of the General Meeting.
- 41.2 If in an election of Persons a majority is not obtained, a second free vote shall be taken. If again a majority is not obtained, further votes shall be taken until either one Person obtains a majority or the election is between two Persons only, both of who receive an equal number of votes. In the event of such further elections (not including the second free vote), each election shall be between the Persons who participated in the preceding election, but with the exclusion of the Person who received the smallest number of votes in that preceding election. If in a preceding election more than one Person received the lowest number of votes, the lot shall decide that of these Persons should not participate in the new election. If there is a tie of votes in an election between two Persons, it shall be decided by lot who is elected, without prejudice to the provision of the following paragraph of this Article 41.
- 41.3 In the event of a tie of votes in an election from a binding list of candidates, the candidate whose name appears first on the list shall be elected.
- 41.4 If there is a tie of votes in a vote other than a vote for the election of Persons, the proposal is thus rejected.
- 41.5 All votes may be cast orally. The chairman is, however, entitled to decide a vote by a secret ballot. If it concerns an election of Persons, also a Person present at the meeting and entitled to vote can demand a vote by a secret ballot. Voting by secret ballot shall take place by means of secret, unsigned ballot papers.
- 41.6 Abstentions and invalid votes shall not be counted as votes cast.
- 41.7 Voting by acclamation shall be possible if none of the Persons present and entitled to vote objects against it.

41.8

Furthermore, the provisions of the Section 2:13, subsections 3 and 4, and Section 2:117 of the Dutch Civil Code shall apply to General Meetings of Shareholders and the adoption of resolutions therein.

Article 42. Meeting of Holders of Shares of One Class.

42.1

The Supervisory Board or the Board of Management shall convene meetings of holders of shares of one class. The meetings shall be held as often as the Supervisory Board or the Board of Management deems necessary, and also whenever such is required in accordance with the law or these Articles of Association.

42.2

With regard to these meetings, the provisions regarding General Meetings of Shareholders shall, to the extent possible, apply.

42.3

Resolutions of the holders of preference shares and priority shares may also be adopted in writing without holding a meeting, provided they are adopted by the unanimous vote of all holders of preference shares or priority shares, respectively, entitled to vote.

CHAPTER XII. NOTICES AND OTHER COMMUNICATIONS.

Article 43.

43.1

All notices of General Meetings of Shareholders, all announcements concerning dividends and other payments and all other communications to Shareholders shall be effected by means of a notice in a national daily paper and in the Euronext Official Price List, without prejudice to the provisions of Section 2:96a, subsection 4, of the Dutch Civil Code.

43.2

Where used in paragraph 1, the term "Shareholders" shall include the beneficiaries of a life interest and pledgees to whom the voting rights on shares accrue.

CHAPTER XIII. AMENDMENT OF THESE ARTICLES OF ASSOCIATION; DISSOLUTION.

Article 44. Amendment of these Articles of Association; Dissolution; Statutory Merger or Demerger.

44.1

A resolution of the General Meeting to amend these Articles of Association, to dissolve the Company or to merge or demerge the Company within the meaning of Title 7, Book 2 of the Dutch Civil Code, shall only be adopted on a proposal of the Supervisory Board. To the extent an amendment shall affect the rights of the Priority the proposal to amend the Articles of Association shall require the approval of the Priority.

44.2

When a proposal to amend these Articles of Association or to dissolve the Company is to be submitted to the General Meeting of Shareholders, such must be mentioned in the notice of the General Meeting of Shareholders and, if an amendment to these Articles of Association is to be discussed, a copy of the proposal, setting forth the text of the proposed amendment verbatim, shall at the same time be deposited for inspection at the Company's office and in Amsterdam at the office of a paying agent as referred to in the Euronext Listing Rules, such paying agent to be designated in the notice of the meeting, and shall be held available for Shareholders as well as for beneficiaries of a life interest and pledgees to which the voting rights on share accrue, free of charge until the end of the meeting.

Article 45. Liquidation.

45.1

In the event of dissolution of the Company by virtue of a resolution of the General Meeting, the Board of Management shall be charged with the liquidation of the business of the Company and the Supervisory Board with the supervision thereof.

45.2

During liquidation, the provisions of these Articles of Association shall remain in force as far as possible.

45.3

From the balance remaining after payment of debts there shall first, as far as possible, be transferred to the holders of preference shares, in proportion to the aggregate nominal value of the preference shares held by each of them:

(a)

an amount equal to any dividend arrears as referred to in Article 31, paragraph 1, of these Articles of Association which shall then be calculated over the period ending on the day on which the liquidation payment shall become payable; and

(b)

the nominal value paid on the preference shares.

Subsequently, the nominal value paid on the priority shares shall be paid to the holders of the priority shares.

45.4

The balance then remaining shall be transferred to the holders of ordinary shares in proportion to the total number of ordinary shares held by each of them.

45.5

The liquidation shall otherwise be subject to the provisions of Title 1, Book 2 of the Dutch Civil Code.

CHAPTER XIV. FINAL AND TRANSITIONAL PROVISIONS.

Article 46. Authority to Issue Shares.

The duration of the authority of the Board of Management to issue shares and to grant rights to subscribe for shares as provided for in Article 7 of these Articles of Association, shall be fixed on five years, effective as of the ninth day of October two thousand. The authorisation concerns all non-issued shares of the authorised capital as it reads now or shall read at some point in time. The same applies to the authorisation of the Board of Management to limit or exclude the right of pre-emption, as provided for in Article 8 of these Articles of Association.

Finally, the person appearing has declared:

Issued Capital.

At the time the foregoing amendment of the Articles of Association takes effect, the issued capital of the Company equals, eight million sevenhundred fifteen thousand sixhundred eighty-two euro and eighty eurocent (EUR 8,715,682.80), divided into thirty-six million threehundred fifteen thousand threehundred thirty-five (36,315,335) ordinary shares with a nominal value of twenty-four eurocent (EUR 0.24) each and ten (10) priority shares with a nominal value of twenty-four eurocent (EUR 0.24) each.

*_*_*_*_*

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[Exhibit 1.2](#)

EMPLOYMENT AGREEMENT (translation from Dutch)

Between:

Introgene B.V. (now Crucell Holland B.V.) a private limited liability company, hereinafter referred to as Introgene;

And:

R.H.P. Brus;

Whereas:

Introgene is a starting biotechnology company with a focus on growth;

Introgene requires an executive who is capable now and in the future to sell and acquire technology;

Mr. Brus has the commercial skills and is willing to make his skills available for Introgene;

Mr. Brus is available to dedicate himself on a national and international level for Introgene and is not affiliated to any other third party in that respect;

Mr. Brus acknowledges that Introgene operates in a highly confidential environment, with regard to research, development as well as from an organizational, corporate and scientific point of view;

Mr. Brus has agreed to relocate as soon as possible to the vicinity of Leiden, the Netherlands.

Have agreed as follows:

1.

Function:

Mr. Brus will be employed by Introgene as Director Business Development. He is responsible for any and all Business Development activities the design and execution thereof. He reports to the managing director. The function includes frequent travel and staying abroad.

2.

Duration:

The employment agreement commences on 15 January 1997, or the sooner as may be agreed upon between the parties, for an indefinite period of time. The first two months are considered as a probation period.

3.

Labor times;

The function requires full dedication above and beyond ordinary office hours.

4.

Salary and holiday allowance:

The salary of Mr. Brus is [deleted] gross per annum. Inclusive holiday allowance, and shall be made payable to a designated account by Mr. Brus in twelve equal installments.

5.

Other benefits:

Introgene is in preparation of a collective pension arrangement in line with current standards.

Introgene shall pay DFL [deleted] to Mr. Brus for a sickness insurance to be taken out by Mr. Brus.

Mr. Brus is eligible to participate in Introgene's option plan. He will be granted 50,000 options with an exercise price to be determined against the value of the share price on 15 January 1997.

Introgene will provide Mr. Brus with a loan in the amount of DFL [deleted] to be repaid within one year. The loan will be immediately repaid at first call of Introgene at their sole discretion.

6.

Expenses:

Introgene shall provide for a monthly fixed expense payment in the amount of DFL [deleted] to reimburse Mr. Brus for ordinary small business expenses. Introgene shall refund all other expenses incurred in the ordinary course of business, subject to properly recording of such expenses in accordance with Company policy.

Mr. Brus shall be compensated for business travel with his own car in the amount of DFL [deleted] per kilometer.

As long Mr. Brus has not found a new home in the vicinity of Leiden, Introgene shall compensate, with a maximum of three months, for housing expenses with a maximum amount of DFL [deleted].

Reasonable relocation expenses shall be reimbursed by Introgene, including travel expenses of Mr. Brus' family on economy class level.

All other relocation expenses shall be reimbursed with a maximum of DFL [deleted].

All expenses have a gross nature. At Introgene's sole discretion payments shall be made on a gross or net basis.

7.

Holidays:

Mr. Brus is eligible to take 25 holidays per annum.

8.

Sickness and Disability;

Notwithstanding article 7A:1638c Dutch Civil Code, Introgene continues to pay Mr. Brus' salary for a period of 52 weeks during sickness. Regarding the calculation of the periods of sickness they are deemed to be aggregate and with an interruption of less than 4 weeks.

Introgene shall be liable for the conclusion of employment disability insurance, on terms to be mutual agreed upon.

9.

Other activities:

Mr. Brus shall not have during his employment other business activities, regardless whether they are paid or not, without express prior written permission.

Notwithstanding the foregoing Mr. Brus shall not, during his employment and for a period of one year thereafter, without prior written permission, apply or have any involvement directly or indirectly with the application of patents or other intellectual property in the areas that Introgene is active in. In case of breach by Mr. Brus he will be held liable for a penalty of DFL [deleted].

10.

Confidentiality:

Mr. Brus shall, both during his employment as after termination of this agreement, keep confidential any and all information that came in his possession as a result of his employment.

In case of breach Mr. Brus will be held liable for an amount of DFL [deleted], multiplied with DFL [deleted] per day that the violation continues.

11.

Non-Compete

Mr. Brus shall for a period of one year after termination of this agreement not be active whatsoever in the field of Introgene's business, regardless whether these activities are current or in preparation.

Signed in two original copies:

Introgene B.V.

R.H.P. Brus

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[Exhibit 4.6](#)

[EMPLOYMENT AGREEMENT \(translation from Dutch\)](#)

EMPLOYMENT AGREEMENT

The undersigned,

CRUCCELL HOLLAND BV, having its offices at Archimedesweg 4, 2333 CN, Leiden, (hereinafter referred to as "Crucell"),

and

Prof. Dr. J. Goudsmit, now residing at Koninginneweg 4, 1075 CX Amsterdam, (hereinafter referred to as Employee),

WHEREAS

Crucell is a leading biotechnology company, principally engaged in the discovery and development of biopharmaceutical products that utilize the immune system to combat diseases.

Crucell is a subsidiary of Crucell N.V., a public limited liability company according to the laws of the Netherlands with a public listing on Amsterdam stock exchange Euronext N.V. and Nasdaq, New York.

Crucell has previously employed Employee as Senior Vice-President Vaccine Research as per September 1, 2002 and now wishes to employ the Employee as Executive Vice President & Chief Scientific Officer as per the Effective Date.

Employee has stated that he is fully entitled and available to serve Crucell nationally and internationally and that he has, in that respect, no restrictions or obligations with respect to anybody;

Employee is fully aware that the business of Crucell requires extreme confidentiality as to everything that is created, developed, prepared, investigated scientifically organisationally, economically, as well as commercially;

Employee and Crucell wish to ratify and confirm the Employee's new position and associated employee benefits. The underlying employment agreement will replace the former employment agreement with Crucell. The number of years of service of Employee ("the seniority") at Crucell will be respected under this new employment agreement;

HAVE AGREED AS FOLLOWS:

DUTIES

- 1.1. Employee will be employed by Crucell as Executive Vice-President & Chief Scientific Officer. The Employee will report to the President & Chief Executive Officer of Crucell and will be a member of the Executive Committee. The function may include travelling and staying abroad. Employee is expected to use his particular knowledge in medical research, including but not limited to vaccine research and if possible, for the creation of industrial or intellectual property rights such as rights attached to inventions.
- 1.2. Employee accepts that he shall also perform duties other than the ones which are considered his usual duties if such performance may be reasonably expected from him.

COMMENCEMENT, DURATION AND TERMINATION

- 2.1 The employment shall commence on September 1, 2002, and will be entered into for an indefinite term. For the avoidance of doubt, this employment contract cancels and supersedes all previous employment contracts, between Crucell and the Employee, including but not limited to the employment contract dated August 29, 2001. However it is agreed that the number of years of service of the Employee since September 1, 2001 ("the seniority") at Crucell will be respected under this employment agreement.
-

2.3. The employment agreement shall in any event and without prior notice expire at the end of the month in which Employee reaches the age of sixty-five.

2.4. Notice will be given by both parties in writing, with effect as per the end of a calendar month. The term of notice is six months for Crucell and three months for Employee.

HOURS OF WORK

3.1. The function requires total dedication during and beyond office hours.

REMUNERATION AND HOLIDAY ALLOWANCE

4.1. Employee shall receive a gross annual salary of Euro 320,000. The gross salary includes statutory holiday allowance of 8%, to be paid in the month of May each year. The salary, net of the statutory holiday allowance, is payable in equal instalments, at the end of each month, to the bank account which will be indicated by Employee. The holiday allowance shall be accrued on a monthly basis by reserving a sum equal to 8% of the monthly income received by the Employee.

FRINGE BENEFITS

5.1. Employee is allowed to participate in the corporate pension plan of Crucell. Crucell warrants that the terms and conditions of Employees' pension plan shall in all material aspects be equal to and therefore not less advantageous than the current pension plan(s) of Crucell's Chief Executive Officer. Main terms of the pension plan shall consist of an agreed maximum pensionable salary of Euro 226,890, inclusive the yearly indexation and Employee contribution of 6% of the applicable pension basis ("pensioengrondslag"). The advisory costs with respect to such pension plan shall also be borne by Crucell. Crucell shall assist the Employee in terminating or transferring accrued pension rights with his current pension plan.

5.2. Crucell shall reimburse 75 percent of health care insurance premiums to Employee.

5.3. Employee is granted the right to participate in Crucell's applicable option plan. As evidence of the Employee's promotion to Executive Vice-President & Chief Scientific Officer, the Employee receives as at September 20, 2002 (the "Date of Grant") 100,000 additional options (the "Grant") Crucell N.V. at the Stock Exchange of Euronext N.V. and NASDAQ and associated Stock Appreciation Rights. The option exercise price will be established in euro's, based on 117% of the average price of the share Crucell N.V. at the close of market on the three trading days on the official market of the stock market of Euronext N.V. in Amsterdam (EAX) prior to the Date of Grant. The option grant will exclusively be governed by Crucell's applicable option plan. The Stock Appreciation Rights grant will be exclusively governed by Crucell's applicable SAR plan.

5.4. For greater certainty the Employee accepts that any compulsory tax withholdings related to or as a result of his rights under this section are for his account.

5.5. To the extent permitted by Dutch or US security laws is the Employee entitled to a director's loan, bearing the same interest rate, and under the same terms and conditions of other director's loans, equal to the amount of taxes to paid by Employee in connection with the Grant.

EXPENSES

6.1. Crucell shall reimburse Employee necessary reasonable business expenses after approval of the specifications. Each month, the Employee will receive a minimum net fixed expense allowance in accordance with Crucell Holland's expense allowance policy.

6.2. The Employee is entitled to a company car in accordance with Crucell's applicable company car policy.

6.3.

All reimbursements are subject to the right of Crucell to restrict to the amount(s) that is or will be allowed by tax regulations or, at the choice of Crucell, to withhold possible premiums and taxes due, at Employee's expense.

HOLIDAYS

7.1

Employee shall be entitled to paid holidays with pay in each calendar year at a rate of 30 working days. Employee shall be obliged to take these holidays in consultation with, and after approval of, Crucell. Holiday leave which has not been taken by the Employee can be transferred to a following year, but shall lapse in accordance with the statutory five-year term of prescription after expiry of the calendar year in which the entitlement arose.

ILLNESS AND DISABILITY

8.1.

If the Employee is unable to perform his duties agreed owing to illness, Crucell shall pay 100% of his agreed wage for a period of 52 weeks. In this provision, wage is understood to mean the wages referred to in article 4 plus the allowances referred to in article 5. Periods of illness are calculated together if intervals are shorter than four weeks.

8.2.

Employee will participate in Crucell's corporate disability insurance plan. The premiums are for the account of Crucell.

NO SIDELINES

9.1.

Except for:

(i)

the duties related to the Employee's chair at the "Amsterdam Medisch Centrum" on a "*nul aanstelling*" basis for which duties Employee will be granted a paid absence leave for a maximum of 24 days per year, assuming these days will be divided proportionally over the year.

(ii)

his involvement with the International AIDS Vaccine Initiative ("IAVI"), for which involvement the Employee will receive a paid absence leave of 12 days per year, excluding travelling days.

(iii)

the involvement of Employee as member of de Council of Scientific Advise of Prima Gen, a company based in Amsterdam,

(iv)

the involvement in reviewing scientific papers,

Employee shall during the employment refrain from having any interest in, or conducting of any outside commercial, outside business or outside scientific activities, with or without remuneration, without the prior written consent of Crucell, such consent not unreasonably to be withheld.

9.2

The remuneration for the duties/involvement of/in the activities mentioned under (i), (ii), (iii) and (iv), if any, shall be for the Employee and discussed and reported to Crucell's Chief Executive Officer.

9.3

For avoidance of doubt the activities referred to under (iii) and (iv) shall be performed in the Employees spare time.

CONFIDENTIALITY

10.1.

Except as required by law or to the extent applicable to information that is in the public domain otherwise than through unauthorised disclosure by the Employee. Employee is fully aware and acknowledges that, during the employment as well as thereafter, strict secrecy in respect of all matters relating to Crucell, organisational, commercial, and scientific, all in the broadest sense, is necessary. This obligation is not restricted to relations with third parties but includes other employees of Crucell in so far the proper performance of the duties of employee does not require disclosure.

10.2. Notwithstanding Clause 13.1, every material violation of section 10.1. may be referred to a competent Dutch court and appropriate damages and/or legal action requested.

NON COMPETITION

11.1 Employee shall for a period of one year after the end of the employment fully refrain from any business wise activity, including any (whether or not for payment) involvement with business wise activities, directly or indirectly, relating to the commercial application of discovery and development of biopharmaceutical products that utilize the immune system to combat diseases within the fields Crucell acts, has acted or prepares to act on at the moment the employment ends.

11.2 Furthermore Employee shall strictly refrain, during the employment as well as during one year thereafter, without the prior written consent of Crucell, from any involvement with the creation, the application for and the recording of intellectual property rights beyond his proper performance under the employment or, after the end thereof, the creation, the application for and the recording of intellectual property rights concerning the existing or future field of activities of Crucell.

11.3 Notwithstanding Clause 13.1, every material violation of sections 11.1 and 11.2 may be referred to a competent Dutch court and appropriate damages and/or legal action requested.

INTELLECTUAL AND INDUSTRIAL PROPERTY RIGHTS

12.1. Employee shall inform Crucell forthwith of every invention, procedure, publication, design, model and in general every creative result in the field of industrial or intellectual property attained by employee, if and to the extent that it relates to Crucell's business activities both in the Netherlands and abroad. If the industrial and intellectual property rights attaching to the invention, etc. do not automatically accrue to Crucell by virtue of the employment relationship, Employee shall at Crucell's first request transfer such rights to Crucell and co-operate fully in recording such rights in the name of Crucell as exclusive owner, all at the expense of Crucell.

12.2. Employee hereby irrevocably appoints Crucell as his agent for the purpose of in his name preparing all documents and performing all other acts necessary for the implementation of the provisions of this article and Crucell is hereby authorised to appoint a sub-agent for the implementation of the foregoing.

12.3. Employee acknowledges that his salary includes reasonable compensation for (his contribution to) the creation of intellectual and industrial property rights.

SEVERANCE PAY UPON TERMINATION OF EMPLOYMENT CONTRACT

13.1 If the Employee is dismissed by Crucell, parties will leave it to the decision of the competent court as to what the amount of severance pay shall be. However, In any case the severance pay granted by the court shall be increased with the amount of salary that the Employee would have received, should the notice period of article 2.4 have been observed by Crucell.

13.2 Without prejudice to the provision referred to in the previous paragraph, the minimum severance pay shall be at least equal to a year salary excluding holiday allowance, if the dismissal of the Employee is due to a merger or a take over of Crucell, either directly or indirectly.

LAW

14.1 This agreement shall be governed by and construed in accordance with the laws of the Netherlands. All disputes arising out of or in connection to this Agreement shall be referred to the competent Dutch court.

EXECUTED on October 25, 2002, in Leiden, the Netherlands and effective as per the Effective Date in duplicate,

For and on behalf of
Crucell Holland B.V.

Employee

By: Crucell N.V.

By:

Title: Director

Name: J. Goudsmit

By:

Name: Domenico Valerio
Title: President & Chief Executive Officer

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[Exhibit 4.7](#)

[EMPLOYMENT AGREEMENT](#)

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Exhibit 8.1

List of Subsidiaries of Crucell N.V.

Legal Entity	Country of Registration
100% subsidiary Crucell N.V.: ChromaGenics B.V. (Amsterdam)	The Netherlands
100% subsidiary Crucell N.V.: Crucell Holland B.V. (Leiden)	The Netherlands
100% subsidiary Crucell Holland B.V.: U-BiSys B.V. (Utrecht)	The Netherlands
20.8% subsidiary Crucell Holland B.V.: Galapagos Genomics N.V.	Belgium (Mechelen)

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[Exhibit 8.1](#)

[List of Subsidiaries of Crucell N.V.](#)

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[Exhibit 12.1](#)
[Certification of Chief Executive Officer](#)

Certification of Chief Financial Officer

I, Leonard Kruimer, certify that:

1. I have reviewed this annual report on Form 20-F of Crucell N.V.;
2. Based on my knowledge, this annual report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this annual report;
3. Based on my knowledge, the financial statements, and other financial information included in this annual report, fairly present in all material respects the financial condition, results of operations and cash flows of the company as of, and for, the periods presented in this annual report;
4. The company's other certifying officer and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) for the company and we have:
 - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the company, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this annual report is being prepared;
 - b) Evaluated the effectiveness of the company's disclosure controls and procedures and presented in this annual report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - c) Disclosed in this report any changes in the company's internal control over financial reporting that occurred during the period covered by this report that has materially affected, or is reasonably likely to materially affect, the company's internal control over financial reporting; and
5. The company's other certifying officer and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the company's auditors and the audit committee of the company's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the company's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the company's internal control over financial reporting.

Date: April 14, 2005

By: _____ /s/ LEONARD KRUIMER

Name: Leonard Kruimer
Title: Chief Financial Officer

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[Exhibit 12.2](#)

[Certification of Chief Financial Officer](#)

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[Exhibit 13.1](#)

[Annual Certification Pursuant to Section 906 of the Sarbanes–Oxley Act of 2002](#)

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