

Report of the Management Board

Overview of the year

The year 2008 was truly unique for Crucell as we achieved net profit for the first time in the history of the Company. In addition we exceeded our revenue targets, considerably improved our gross margin and were cash flow positive. It is Crucell's ambition to deliver on promises and we clearly exceeded the targets set at the beginning of the year. Our 2008 financial highlights include:

- Growth of 33% in revenues and other operating income in 2008;
- Net profit of € 14,586 in 2008 compared to a net loss of € 42,910 in 2007;
- Gross margin for the year improved to 45% in 2008 compared to 34% in 2007; and
- Positive cash flow of € 7,721 increasing the 2008 year-end cash position to €170,969.

Our mission is to develop, produce and market vaccines and antibodies that prevent or treat infectious diseases. We have a fully-integrated infrastructure for in-house development, production and marketing of vaccines, and we are now leveraging our knowledge in this area to enter the antibodies market for infectious diseases. Our business strategy is based on the following business drivers:

- Leveraging presence of our marketed vaccines in public and private markets;
- Building a product pipeline with sustainable competitive advantage; and
- Building upon ongoing technology licensing programs.

The weakness of the global economy in 2008 is a challenge for many companies worldwide.

The ongoing financial crisis became prominent in September 2008 with the failure or near-failure of several United States and European based financial institutions. The resulting deterioration in financial and market conditions spread around the globe. In recent months, the financial crisis has adversely affected businesses in many industries and geographical areas all over the world at an unexpected pace.

Despite the weak global economic climate we achieved all targets we set ourselves for the financial year 2008. Our success depends in part on our solid customer-base, which is relatively unaffected by deterioration in the global economy, since many of our customers are governmental agencies or supranational organizations. We do not expect our business will be significantly affected by the weak global economy in 2009.

Leveraging presence of our marketed vaccines

For the full year 2008, product sales were € 226,055, representing sales of paediatric vaccines (49%), travel and endemic vaccines (25%), respiratory vaccines (14%) and other products (12%). Our product sales grew by € 48,486 or 27.3%. The increase is primarily attributable to increased sales of our paediatric vaccines, specifically Quinvaxem, of € 33,668 and travel and endemic vaccines of € 8,290.

Quinvaxem is our fully liquid pentavalent vaccine against five important childhood diseases that is approved by the WHO. In 2008 we more than doubled the production and we were able to continue the success of Quinvaxem as sales grew from 21.3 million units in 2007 to 39.6 million units in 2008. In anticipation of the expected further growth of Quinvaxem in 2009, we continued to build up stock of Quinvaxem in the fourth quarter of 2008.

In 2008, the Chinese authorities approved Hepavax-Gene, our recombinant Hepatitis B vaccine, which is a significant advancement in the expansion of Crucell's business in the highly strategic Chinese vaccine market. This will accelerate the growth of our Chinese operations.

Operations

In February 2008, our Chief Operating Officer, Cees de Jong, was nominated to join the Management Board. This nomination was approved by our shareholders at the Company's annual general meeting on May 30, 2008. Cees joined Crucell in September 2007 and he was already part of Crucell's Management Committee, prior to his nomination to the Management Board.

In 2008, we also attracted several new senior managers to further improve the quality of our operations. During 2008 we strengthened the manufacturing organization and we were able to improve our performance significantly as yields of important production processes increased and scrap rates decreased. Expenses on operations were more or less stable compared to 2007 despite a significant increase in production volumes.

All our facilities were audited multiple times during the year by customers and/or regulatory authorities. All audits were successful, confirming our compliance with relevant rules and regulations. In Bern, Switzerland, we successfully refurbished our MoRu-Viraten (MR) filling line and obtained approval from Swissmedic to recommence production. In Madrid, Spain, we installed a new filling line for syringes, bringing the total capacity of our dedicated fill/finish center in Spain to approximately 100 million syringes per annum. The Spanish authorities audited and approved the new line in December 2008.

In October 2008, we announced that an agreement was reached to relocate our Korean production facility, that manufactures Quinvaxem and Hepavax-Gene, from the Shingal site in Yongin City to the Incheon, Free Economic Zone. We agreed on the time-line and conditions of this relocation with all parties involved, facilitating a smooth transition to the new production facility. The new facility will enable the further growth and efficient production of Quinvaxem and Hepavax-Gene. All litigation surrounding our production facility has been settled.

In August 2008, we announced the intention to move Dukoral and rCTB bulk production, formulation and fill/finish activities from Sweden to other sites within the Crucell organization. The Group is currently conducting a feasibility study to determine the scope and timing of a potential move. The research activities conducted at our Swedish site were discontinued in 2008 and are now concentrated in Leiden, the Netherlands.

We entered into an exclusive vaccine development agreement with Wyeth Pharmaceuticals in which we will be responsible for the development and manufacturing of certain components of a vaccine for use by Wyeth in clinical studies. Wyeth will be responsible for the clinical development of the

vaccine. The development activities will take place in Crucell's dedicated vaccine manufacturing facilities in Bern, Switzerland, which had been fully impaired in 2006, enabling a partial reversal of that impairment in 2008.

Product pipeline with sustainable competitive advantage

Our rabies candidate product achieved positive preliminary results in the phase II study that was carried out in the US. No adverse events were reported and the study confirmed the neutralizing activity of the monoclonal antibody product against the rabies virus. A second phase II clinical study evaluating the monoclonal antibody cocktail in combination with a vaccine in healthy children and adolescents was conducted in the Philippines from May to October 2008. Final data from this study is expected to become available in the first half of 2009. An additional phase II study in healthy adults evaluating Crucell's monoclonal antibody in combination with another rabies vaccine is scheduled to start in India in the second quarter of 2009.

For our Ebola and Marburg vaccine research we secured a contract with the US National Institute of Allergy and Infectious Diseases (NIAID), which is part of the National Institutes of Health (NIH) aimed at advancing the development of Ebola and Marburg vaccines, the ultimate goal being a multivalent filovirus vaccine. The contract provides us with funding of up to US Dollar (\$) 30 million, with additional options that may be triggered at the discretion of the NIH worth a further \$ 40 million. The phase I study of an adenovirus 5 (Ad5)-based Ebola vaccine, being developed in partnership with the Vaccine Research Center (VRC) of the NIAID/NIH, showed safety and immunogenicity. Based on these results, a second phase I study of an Ebola and/or Marburg vaccine is anticipated. The study will use alternative adenovirus vectors, which are able to bypass pre-existing immunity against Ad5.

Our research on a tuberculosis vaccine in collaboration with Aeras is ongoing. In October 2008, Crucell and the Aeras Global TB Vaccine Foundation announced the start of a phase I clinical trial in Kenya. The main parameters of the study are to test the safety of the vaccine candidate in healthy adults. We also started the enrollment of the first phase II study of the vaccine candidate, which will be conducted in South Africa by the University of

Cape Town Lung Institute in conjunction with the South African Tuberculosis Vaccine Institute.

Our malaria research in collaboration with the NIAID/ NIH is progressing as we are carrying out a phase I trial in the US. The study is being carried out at two sites: Vanderbilt University in Nashville, Tennessee, US, and Stanford University in Palo Alto, California, US. The first three groups have been enrolled and ongoing safety monitoring has revealed no significant safety concerns to date, but formal analysis awaits. Enrollment for the fourth and final group of volunteers is ongoing.

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

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

Registration submission of Flavimun, our yellow fever vaccine in Switzerland was completed in the first quarter of 2009. Registration submission in Germany is expected in 2009.

Unique technologies for licensing business

In 2008, our license revenues grew by € 17,991 or 147.3%. The increase is mainly due to revenues generated by our collaboration with sanofi pasteur.

In 2008, Crucell signed licensing agreements with Abraxis Bioscience, Inc., Affitech AS, Arana Therapeutics Ltd, Bioceros, Biochrom, Cangene Corp., Celltrion, Inc., Gedeon Richter, GlaxoSmithKline, CSL Ltd., Lonza, Medarex Inc., MorphoSys AG, Profibrix B.V., Synthon B.V., Talecris Biotherapeutics and Toyobo Gene Analysis Co. Ltd.

We signed two exclusive, commercial license agreements with Talecris Biotherapeutics for two undisclosed and specific proteins and the exclusive rights to produce those proteins using the PER.C6 cell line. In total, we received upfront payments of \$ 4 million upon the execution of the agreement and will be eligible for milestone payments of approximately \$ 50 million more.

There were also positive developments for our intellectual property. We were successful in opposing European patents of our competitors as we managed to obtain complete revocations of European patents owned or controlled by GenVec, Genentech, Baxter, Novartis Vaccines & Diagnostics, Wellcome Foundation (GlaxoSmithKline (GSK)), and others. In addition, we obtained a favorable decision from the South-Korean Supreme Court in the longstanding invalidity law suit in South Korea against GSK's multivalent Hepatitis B virus vaccine patent. These developments further paved the way for Crucell's pipeline development activities and marketed products. Conversely, we were successful in defending our own PER.C6 and AdVac patents against attacks by its competitors. Except for one PER.C6 patent that has been maintained in amended form and is now pending before the board of appeal, all PER.C6 patents have survived opposition before the European Patent Office essentially intact.

The following technological progress was achieved during 2008:

- We achieved important advances in antibody production using our PER.C6 technology platform together with our partner DSM Biologics. By employing the PER.C6 human cell line and proprietary XD™ technology, we achieved a record yield of over 27 grams per liter of IgG antibodies. In addition the high-titer fed-batch process was scaled up to 250 liters by DSM Biologics scientists at their GMP facility in Groningen, The Netherlands;

- Our PER.C6 technology licensee Ark Therapeutics has entered a phase III study with its product Trinam. Ark Therapeutics is the first of our licensees to enter into a phase III study with a product produced on Crucell's PER.C6 human cell line; and
- We announced that the novel recombinant adenovirus serotype 26 (rAd26) vector, which is jointly developed by Crucell and the Beth Israel Deaconess Medical Center (BIDMC) in the US, will be used in a phase I clinical study to test a new HIV vaccine. The rAd26 vector is specifically designed to avoid pre-existing immunity to the more commonly used adenovirus serotype 5 (Ad5), which has recently shown limitations as an HIV vaccine vector. This clinical trial is the first 'in man' study of this newly developed vector, which could provide a solution to problems seen in previous HIV vaccine trials. The rAd26 vaccine is the first HIV vaccine candidate to emerge from the Integrated Preclinical/Clinical AIDS Vaccine Development (IPCAVD) program.

In November 2008, the leading scientific journal 'Nature' published a study that demonstrated the value of our alternative adenovirus serotype technologies. Using Crucell's AdVac vaccine technology and PER.C6 manufacturing technology, scientists engineered the rare adenovirus serotypes Ad26 and Ad35 to express a protein of SIV, the primate equivalent of HIV. We have developed rare serotype adenoviral vectors, such as rAd26 and rAd35, to provide more potent prime-boost vaccine regimens. The study, which investigated the immunogenicity and protective efficacy of different vaccination regimes using rAd26, rAd35 or rAd5 as a primer, followed by a boost with rAd5, showed that in particular the rAd26/rAd5 combination elicits a strong T-cell immune response and provides protection against the HIV-like virus in primate subjects. We have several vaccines in development using alternative rAd26 and rAd35 vectors, including vaccines against malaria and tuberculosis.

For further details on licenses and licensees please see 'Information on the Company – Overview of Licensees and Partners' in this Annual Report.

Subsequent events

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

Outlook 2009

The key to our strategy is continued growth. The outlook for 2009 is promising as we expect revenue and other operating income to grow, operating profits to increase significantly and to achieve a solid cash flow despite significant investments. Our Healthy Ambition program has a clear focus on achieving operational excellence and is on track to realize cost savings of € 30 million by the end of 2009. We do not expect our business to be adversely affected in 2009 by the weak global economy resulting from the continuing international financial crisis.

In 2009, we will focus on continued growth.

- We expect our combined full-year 2009 total revenue and other operating income to grow by 20% in constant currencies that are set at a guidance rate of Euro/US Dollar of 1.35;
- Operating profit for 2009 is expected to improve significantly compared to 2008;
- Furthermore, the Company expects solid cash flow despite significant investments in the new facility being built in Korea. These investments are expected to total approximately € 50 million, with the majority of the spending in 2009;
- We do not expect our business to be significantly affected by the weak global economy in 2009; and
- We will pursue key partnerships, focus on progress in clinical development and continue with broadly licensing our technologies.

In the course of 2009, we expect to make further decisions that may impact our income statement. Consequently we cannot comment on expected 2009 results in more detail than described above.

Our Healthy Ambition program has a clear focus on achieving operational excellence. The program works towards exploiting synergies, reducing costs and funding growth. Important elements of the program include: product portfolio optimization, process and infrastructure optimization, network rationalization and further integration and streamlining of various functions. Healthy Ambition is targeting savings of € 30 million by the end of 2009. For 2009, the focus will be on reducing complexity and further streamlining the organization.

We expect continued investments in our manufacturing facilities to ensure that they remain state-of-the-art and continue to meet the highest applicable regulatory standards. In October 2008, we announced that we will relocate our Korean production facility. The investments in the new facility are expected to total approximately € 50 million, with the majority of spending occurring in 2009. We entered into a mortgage loan facility in Korea for an amount of KRW 50 billion to partly finance the investments in the new Korean facility in 2009.

Our continued growth strategy also includes continued investments in R&D to ensure solid progress in clinical development. Both vaccine and antibody research is being focused on combating infectious diseases, with an emphasis on the existing categories of paediatric, travel and endemic, and respiratory illnesses. In addition, we will continue to invest in discovery programs and progress these into the clinical trial phase. Lifecycle investments are required to ensure that we continue to meet the highest regulatory standards and to further improve the lifecycle of our products.

We expect the deal flow from our PER.C6 licensing business to continue. We believe that the number of licenses and the revenue flow from the PERCIVIA joint venture will continue to be significant.

We expect revenues throughout 2009 to be phased similarly to those in 2008. Our cash flow position is expected to deteriorate significantly in the first half of 2009, which is normal due to the seasonality of our business. We build-up inventory in the first half of the year and sell our respiratory and travel vaccine products principally in the second half of the year.