

QUARTERLY UPDATE

Fourth Quarter and Full Year Financial Results Reported

Snapshot

January 25, 2005

Crucell N.V. is a biopharmaceutical company that employs proprietary technology to discover, develop, manufacture, and commercialize vaccines and antibodies targeted at a variety of infectious diseases. The Company utilizes a human cell line production system called PER.C6[®], which may facilitate products with greater safety, efficacy, and cost-efficiency than those currently marketed. Crucell is developing vaccines to treat and prevent influenza, Ebola, West Nile virus and malaria, and is in the discovery stage with a tuberculosis (TB) vaccine and antibodies for rabies and Severe Acute Respiratory Syndrome (SARS). Crucell works with sanofi aventis SA (SNY-NYSE) to develop and commercialize its influenza vaccine; has a Collaborative Research and Development Agreement (CRADA) and vaccine production contract in place with the U.S. National Institutes of Health (NIH) for its Ebola vaccine; and is working with GlaxoSmithKline PLC (GSK-NYSE), New York University (NYU), and the Walter Reed Army Institute of Research (WRAIR) to develop its malaria vaccine, which has been funded up to the clinic by the National Institute of Allergy and Infectious Diseases (NIAID).



Crucell N.V.
Archimedesweg 4
Leiden
The Netherlands
Phone: +031 (0) 71 524 8722
www.crucell.com

Recent Financial Data

Ticker (Exchange)	CRXL (NASDAQ)
Recent Price (01/25/05)	\$13.41
52-Week Range	\$15.37-6.52
Shares Outstanding (mm)	36.3
Market Cap. (mm)	497.51
Average 3-month volume	208,727
Insider +5% Owners	>96%
Institutional Owners	40%
EPS (full year ended 12/31/04)	(\$0.80)
Employees	>200



Key Points

Euros (€) are converted to U.S. Dollars at the December 31, 2004 exchange rate of 1.36440.

- Crucell N.V. reported financial results for the fourth quarter and full year 2004 on January 24, 2005. Total revenue for the quarter increased to \$8.9 million (€6.5 million), compared with \$4.0 million (€3.0 million) for the same period in 2003. Net loss for the fourth quarter 2004 increased to \$9.3 million (€6.8 million), compared with \$8.7 million (€6.4 million) for the same period in 2003. For the full year 2004, revenues were \$30.9 million (€22.6 million), up from \$10.1 million (€7.4 million) in 2003. The Company reported a net loss for 2004 of \$29.1 million (€21.3 million), down from \$31.9 million (€23.4 million) in 2003, notwithstanding a \$5.3 million (€3.9 million) increase in research and development (R&D) expenditures as Crucell continues to step up its core programs.
- During the quarter, Crucell signed new license agreements for its PER.C6[®] technology with Chiron Corporation (CHIR-NASDAQ), Merial Limited, Edwards Lifesciences Corporation (WE-NYSE), and Micromet AG of Germany.
- Crucell's portfolio of proprietary technologies (PER.C6[®], AdVac[®], and MAbstract[®]) form the basis of its product development programs, as well as a lucrative licensing business currently serving more than three dozen other industry participants. Each of Crucell's product programs addresses an important unmet medical need in the area of infectious diseases.
- The Company maintains a solid balance sheet, with a cash position of \$104.7 million (€76.7 million) as of December 31, 2004. Additionally, Crucell has significantly reduced its cash burn rate versus the comparable period last year with \$14.3 million (€10.5 million) cash burn reported as of December 31, 2004, less than half the \$32 million (€23.4 million) recorded in 2003.

Financial Results

Note: Euros (€) are converted to U.S. Dollars at the December 31, 2004 exchange rate of 1.36440.

Fourth Quarter 2004

Crucell N.V. reported financial results for the fourth quarter and full year 2004 on January 24, 2005. Total revenue for the quarter increased to \$8.9 million (€6.5 million), compared with \$4.0 million (€3.0 million) for the same period in 2003. Revenues for the quarter consisted of upfront payments from new contracts as well as annual and other payments on existing contracts.

License revenues amounted to \$3.6 million (€2.6 million), compared with \$2.1 million (€1.6 million) in the fourth quarter 2003; and government grants and other revenues were \$2.6 million (€1.9 million) versus \$1.8 million (€1.3 million) in the same quarter in 2003, reflecting an increase in the number of grant applications the Company has made to support its development programs.

Total research and development (R&D) expenses in the fourth quarter increased to \$10.5 million (€7.7 million), from \$7.5 million (€5.5 million) in the same period last year. Selling, general, and administrative (SG&A) expenses during the quarter were \$5.9 million (€4.4 million), compared with \$3.7 million (€2.7 million) during the same quarter last year.

Net loss for the fourth quarter 2004 increased to \$9.3 million (€6.8 million), compared with \$8.7 million (€6.4 million) for the same period in 2003.

Full Year 2004

For year ended December 31, 2004, revenues increased more than three-fold to \$30.9 million (€22.6 million), compared with \$10.1 million (€7.4 million) in 2003. The more than three-fold increase is primarily attributable to a solid increase in licensing deals and arrangements with third parties, which funded certain of Crucell's development programs. Year-to-date cash burn was \$14.3 million (€10.5 million), representing less than half the cash burn of \$32.0 million (€23.4 million) recorded in 2003.

Total R&D expenses in 2004 were \$35.7 million (€26.1 million), compared with \$30.4 million (€22.3 million) in 2003. SG&A expenses for 2004 were \$20.1 million (€14.7 million), compared with \$10.4 million (€7.6 million) for the same period in 2003. This increase was primarily driven by increases in non-cash expenses of \$6.5 million (€4.8 million). Non-cash expenses consisted of a \$4.2 million (€3.1 million) increase in warrant expenses as a result of share price increases, and a \$2.3 million (€1.7 million) non-cash increase in compensation expense. This is related to a one-time, non-cash reduction of compensation expenses in 2003. The remaining \$3.1 million (€2.3 million) increase in SG&A costs was due to increases in insurance premiums, advisory costs, and compensation expenses over the year.

Net loss for 2004 was \$29.1 million (€21.3 million), or \$0.80 per share (€0.59 per share) compared with a net loss of \$31.9 million (€23.4 million), or \$0.89 per share (€0.65 per share) in 2003. The Company's cash position was \$104.7 million (€76.7 million) on December 31, 2004.

Corporate Growth Strategy

Crucell's strategy for growth is to become a leading biotechnology company in the field of infectious diseases based on the success of its proprietary technologies. The Company is involved in virtually every international vaccine initiative worldwide. Its lead areas of development are summarized below.

- *Malaria.* As part of the CRADA including GlaxoSmithKline, Crucell is developing a recombinant malaria vaccine based on an adenovirus vector carrying the gene for the circumsporozoite protein (CSP) from the malaria parasite, *Plasmodium falciparum*.
- *Influenza.* In an alliance with sanofi aventis, Crucell is developing an inactivated whole virus influenza vaccine based on the PER.C6[®] technology. PER.C6[®] cells are highly susceptible to influenza viruses,

thereby making the production of large amounts of influenza virus vaccine feasible. Two types of influenza vaccine are currently in development: an epidemic vaccine and a pandemic vaccine.

- **Ebola.** In a CRADA with the NIH, Crucell is developing an Ebola vaccine based on its proprietary adenoviral vectors and produced using its PER.C6[®] technology. This recombinant vaccine expresses Ebola viral proteins and provides protection against infection with the Ebola virus.
- **West Nile virus.** Crucell is developing a preventative vaccine for humans based on a chemically inactivated whole West Nile virus. The inactivated whole virus vaccine is produced on Crucell's PER.C6[®] technology. Also, in a separate program, Crucell is collaborating with Israeli Kimron Veterinary Institute in the development of an inactivated whole West Nile virus vaccine for veterinary use. Market authorization was granted in June 2004.
- **HIV.** Through alliances with Merck & Company and with the International AIDS Vaccine Initiative (IAVI), Crucell's technology is playing a vital role in developing an HIV/AIDS vaccine. In October 2002, Crucell entered into an agreement with Merck & Company, in which Merck was granted an exclusive license to use Crucell's PER.C6[®] technology to develop vaccines for the prevention and treatment of HIV/AIDS. Also, in September 2004, Crucell and the IAVI signed an exclusive license agreement to develop an AIDS vaccine based on Crucell's AdVac[®] technology.

Recent Events

- **Crucell Joins Influenza Vaccine Supply (IVS) International Task Force.** On January 14, Crucell announced that it had been accepted as a new member of the Influenza Vaccine Supply (IVS) international task force. The IVS is a specialized group within the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) created in February 2002 to assist business leaders in ensuring adequate flu vaccine production capacity in the event of a pandemic, and to provide advice to health authorities regarding vaccination recommendations and delivery strategies.
- **Crucell Announces Evaluation by Genentech of STAR[™] Technology.** On January 7, Crucell announced that Genentech, Inc. (DNA-NYSE) is currently evaluating its STAR[™] technology for the production of antibodies and proteins. The two companies are investigating whether STAR[™] technology can increase the production of Genentech's proprietary systems. With the first phase of the evaluation successfully completed, Genentech has decided to enter into a second phase, which will test the technology under larger scale production conditions.
- **Crucell Receives European Patent Covering PER.C6[®] for Vaccine Production.** On January 5, Crucell announced the receipt of a patent by the European Patent Office specifically relating to the use of its proprietary PER.C6[®] technology for the production of vaccines. The patent (number: EP 1108787 B1) firmly protects the use of the PER.C6[®] technology for the production of all non-adenoviral viruses, including influenza viruses, for use in veterinary or human vaccines. Further, the patent broadly covers the production of any non-adenoviral virus on E1-immortalized cell lines. This patent also strengthens Crucell's patent position in the emerging field of cell-based vaccines.
- **Crucell Secures €2 Million Grant for Malaria Collaboration from Dutch Ministry of Economic Affairs.** On December 23, Crucell announced that it had received a grant of up to €2 million from the SenterNovem program of the Dutch Ministry of Economic Affairs to support its malaria research and AdVac[®] technology development. The SenterNovem program consists of more than 100 different subsidy schemes targeting high technology, energy, the environment, exports, and international collaboration.

- *CEVEC Acknowledges Crucell Claims in Patent Infringement Hearing.* On December 16, Crucell announced that in the patent infringement action it initiated against CEVEC Pharmaceuticals GmbH, the German Düsseldorf District Court held a first oral hearing on December 15. CEVEC acknowledged Crucell's claims for an injunction as well as further claims for damages and information. The claims were based on the recently granted European Patent for Crucell's PER.C6[®] technology (EP 833 934). Crucell had argued that CEVEC's cell line N52.E6 constituted an infringement of that patent. The court is expected to render an enforceable interim judgment on the basis of CEVEC's acknowledgement in the near future.
- *Milestone Reached in Merck's PER.C6[®]-related investigational HIV Vaccine Program.* On December 15, Crucell announced that Merck & Co., Inc. had met a clinical development milestone in connection with the PER.C6[®] technology licensed to Merck for its investigational HIV program. Merck has started Phase II clinical testing in the U.S., Caribbean, and South America.
- *Candidate for Amsterdam Midkap Index on Euronext.* On November 30, Crucell announced its selection by Euronext Indices B.V. as a candidate for inclusion in the Amsterdam Midkap (AMX) Index. Crucell's inclusion was confirmed on January 1, 2005, to take effect on and from March 2, 2005.
- *Crucell Discovers and Validates Human Monoclonal Antibody Product that Protects Against Rabies in Collaboration with CDC and TJU.* On November 16, Crucell announced the discovery and preclinical validation of an effective monoclonal antibody product for protection against rabies. The Crucell program has been performed in close 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. This new approach may offer an alternative to Human Rabies Immune Globulin (HRIG) that is currently used in combination with a rabies vaccine in the event of exposure to this lethal disease, but which is compromised by cost, availability, and safety concerns.
- *Crucell Signs Agreement with IAVI to Develop AdVac[®] Vector for AIDS Vaccine Program.* On November 12, Crucell and the International AIDS Vaccine Initiative (IAVI) announced the signing of an agreement in which Crucell will develop AdVac[®] vectors for use in IAVI's AIDS vaccine development program. The two organizations also have an exclusive license agreement to develop an AIDS vaccine based on Crucell's AdVac[®] technology.
- *Crucell to Produce West Nile Virus Vaccine for Use in Human Clinical Trials at Netherlands Vaccine Institute.* On November 10, Crucell and the Netherlands Vaccine Institute (NVI) announced the signing of an agreement to manufacture West Nile virus vaccine for use in human clinical trials at NVI's new BSL-3 (Biosafety Level 3) plant. Her Majesty Queen Beatrix of the Netherlands officially opened the plant on November 10.

New PER.C6[®] Licensing Agreements

- *Licensing Agreement with Chiron for PER.C6[®].* On December 22, Crucell announced the signing of a second PER.C6[®] license agreement with Chiron Corporation. The non-exclusive research agreement allows Chiron to use the PER.C6[®] technology in manufacturing alphavirus vectors for its vaccine research programs. Financial details were not disclosed.
- *Licensing Agreement with Edwards Lifesciences.* On November 24, Crucell announced the signing of a PER.C6[®] research license agreement with Edwards Lifesciences Corporation. The non-exclusive agreement allows Edwards to use the PER.C6[®] cell line for research and development of gene therapeutics based on adenoviral vectors. Under the terms of the agreement, Crucell has also granted Edwards access to technical and regulatory support. Financial details were not disclosed.
- *Licensing Agreement with Micromet for Monoclonal Antibody Production.* On November 19, Crucell and DSM announced that they had signed a PER.C6[®] licensing agreement with Micromet AG of Germany. This license agreement allows Micromet to use the PER.C6[®] cell line for evaluating the expression of certain recombinant monoclonal antibody products and subsequent preclinical

manufacturing. Under the agreement, Crucell and DSM will receive a research license payment and annual maintenance fees. Further financial details were not disclosed.

- **Commercial License Agreement for PER.C6[®] for Foot-and-Mouth Disease Vaccines with Merial.** On October 18, Crucell and Merial, a world-leading animal health company, announced that they have entered into a license agreement for the utilization of Crucell's PER.C6[®] technology for the development and commercialization of veterinary vaccines for foot-and-mouth disease (FMD). FMD is a highly communicable disease of production animals and is identified by the U.S. government as a potential bio-terrorism risk. Under the terms of the agreement, Crucell will receive an upfront payment, milestone payments, annual maintenance fees, and royalties on sales of vaccines. Further financial details were not disclosed. In on-going and close collaboration with the U.S. Department of Agriculture, Agricultural Research Service (ARS) Plum Island Animal Disease Center, Merial will further develop FMD vaccines discovered by ARS. These vaccines would be held in reserve for rapid distribution in the event of an accidental or terrorist-caused FMD outbreak.

Full Year 2004 Highlights

Key Candidates

A summary of the status of each of Crucell's key proprietary candidates under development is provided in Table 1.

Category	Description	Development Status
Influenza	Sanofi Aventis and Crucell announced a strategic agreement to develop and commercialize novel PER.C6 [®] -based influenza vaccines.	Clinical trials are set to begin in the third quarter of 2005.
West Nile Virus	The State of Israel granted market authorization for a West Nile virus veterinary vaccine for geese developed by Crucell together with the Israeli Kimron Veterinary Institute. Agreement reached with the Netherlands Vaccine Institute (NVI) for the manufacture of the clinical trial vaccine lots at the NVI's new BSL-3 plant.	Clinical trials of Crucell's human West Nile virus vaccine are set to begin during the fourth quarter of 2005
Malaria	The National Institute of Allergy and Infectious Diseases (NIAID) at the US National Institutes of Health (NIH) agreed to support the development of Crucell's candidate Malaria vaccine. Monkey trial data announced in November 2004 showed excellent immune responses for Crucell's AdVac [®] -based vaccine.	Clinical trials are set to begin in 2006.
Ebola	Experiments performed by the Vaccine Research Center (VRC) of the US National Institutes of Health (NIH) and the US Army Medical Research Institute of Infectious Diseases (USAMRIID) demonstrated that a single dose of Crucell's PER.C6 [®] -based vaccine protects macaque monkeys from Ebola infection.	Clinical trials are set to begin during the fourth quarter of 2005.
Rabies	Crucell discovered an anti-rabies antibody product using its MAbstract [®] technology. The antibody product has proven effective in protecting hamsters against a lethal rabies challenge.	Results of an evaluation of how to proceed with development will be announced in the second quarter of 2005.
SARS	<i>The Lancet</i> medical journal published the results of a study demonstrating that a human monoclonal antibody, discovered with the use of Crucell's MAbstract [®] technology and produced on the PER.C6 [®] cell line, was able to effectively protect ferrets from SARS.	No outbreaks of SARS since early 2004. Product on hold until market need becomes more clear.
Tuberculosis	Crucell and the Aeras Global TB Vaccine Foundation announced a new collaboration on the preclinical and clinical development of candidate tuberculosis (TB) vaccines.	Proof-of-concept results will be announced in the second quarter of 2005.

Source: Crucell N.V.

Corporate Achievements

Crucell reported significant achievements in acquiring a new technology, advancing a key antibody into clinical trials, and achieving a significant development milestone during 2004.

- *ChromaGenics B.V. STAR™*. Crucell completed the acquisition of ChromaGenics B.V., adding its STAR™ technology to Crucell's protein production business. In a Genentech-funded joint evaluation program, Genentech and Crucell are currently investigating whether STAR™ technology can increase the production yields of Genentech's proprietary systems.
- *AME, Inc./Eli Lilly & Company (LLY-NYSE)*. Crucell took the first antibody produced on PER.C6® technology to clinical trials in the U.S. in the first half of 2004.
- *Merck & Company, Inc.* Merck's PER.C6®-based HIV vaccine progressed to the next phase of clinical trials, thereby delivering a milestone payment to Crucell.
- *DSM Biologics Milestone*. Crucell and DSM Biologics achieved the first development milestone pertaining to their protein production collaboration, with the joint development program demonstrating industry-high yields.

Crucell also reported a host of new licensing transactions, advanced its patent positions, and enhanced its supervisory board. Additionally, the Company appointed a new President, CEO, and Chairman this past June.

- *Licensing*. PER.C6® licensing deals were secured by the Crucell-DSM alliance with Biogen Idec (BIIB-NASDAQ), PanGenetics, Merus, Chiron, GlaxoSmithKline PLC, Synergenics LLC/Synco BioPartners Investments, MorphoSys (MPHSF.PK) and Micromet. Crucell also signed further PER.C6® deals with NeoTropiX Inc, ML Laboratories, Wyeth (WYE-NYSE), Vaxin, Merial, Edwards Life Sciences, and Chiron.
- *Intellectual property*. Crucell brought its European patent position in line with its position in the U.S., securing European patents for PER.C6® and AdVac® technology. The first legal proceedings regarding infringement of the PER.C6® patent were subsequently launched against CEVEC. A further European Patent was added in January 2005 specifically relating to the application of PER.C6® for vaccines.
- *Supervisory Board*. Mr. Jan Pieter Oosterveld was appointed to Crucell's Supervisory Board by shareholders. Mr. Domenico Valerio, the Company's founder and former President and CEO, will continue to serve the Company in an advisory role with an emphasis on investor- and public-relations, and not as a member of the Supervisory Board. Mr. Arnold Hoevenaars has been nominated to the Supervisory Board and shareholder approval for his appointment will be sought at the Annual General Meeting on June 2, 2005.
- *Management*. Mr. Ronald H.P. Brus MD was appointed as the new President, CEO, and Chairman of the Management Board of Crucell at the Annual General Meeting of Shareholders on June 3, 2004. In addition, CSO Mr. Jaap Goudsmit MD PhD, and CFO Mr. Leonard Kruimer CPA, were appointed as members of the Company's Management Board.

Background

Crucell is focused on developing vaccines and antibodies to treat and prevent influenza, Ebola, malaria, West Nile virus, and rabies using its proprietary PER.C6[®] technology. To assist in its internal development efforts, Crucell has entered into an agreement to develop and commercialize its influenza vaccine with Aventis Pasteur. The Company also has a Cooperative Research And Development Agreement (CRADA) and vaccine production contract in place with the U.S. National Institutes of Health (NIH) for its Ebola vaccine. Furthermore, Crucell is working with GlaxoSmithKline, New York University (NYU), and the Walter Reed Army Institute of Research (WRAIR) to develop its malaria vaccine, which is fully funded up to the clinic by the National Institute of Allergy and Infectious Diseases (NIAID). Brief details on each of these programs are provided below, with extensive details provided in our base report, the Executive Informational Overview™ (dated May 26, 2004).

Internal Product Development

Influenza. In January 2004, Aventis Pasteur and Crucell entered into a strategic agreement to develop and commercialize novel influenza vaccine products based on Crucell's PER.C6[®] cell line technology. The agreement covers both pandemic and epidemic influenza vaccines, which up to now have been part of Crucell's in-house product development program. The agreement could provide Crucell with a solid position in the vaccine market, provide a more solid overall financial position in the near- as well as long-term, free up resources for its other in-house development programs, and provide technology recognition for PER.C6[®] as the industry standard for vaccine production.

- *Update.* The joint project teams that have been established with Aventis are in place both in Leiden as well as Lyon, France, with technology transfer having been achieved. Clinical trials are set to begin in the third quarter 2005.

Ebola. In May 2002, Crucell signed a CRADA with the Vaccine Research Center (VRC) of the U.S. NIH and the U.S. Army to jointly develop and manufacture a preventative Ebola vaccine. Additionally, Crucell signed a manufacturing contract with the NIH to develop and manufacture an outbreak vaccine against Ebola. Both vaccines are based on Crucell's PER.C6[®] technology. Due to the deadly nature of this virus and the fact that no vaccine or therapy is presently available, the Ebola virus is on the NIAID, Centers for Disease Control and Prevention (CDC), and U.S. Department of Defense Category "A" list of bioterror agents. In August 2002, the CRADA with the VRC-NIH covering a preventative Ebola vaccine was extended to cover the development of vaccines against other hemorrhagic fever viruses (marburg and lassa) as well.

- *Update.* In June 2004, Crucell demonstrated that a PER.C6[®]-based vaccine was able to protect monkeys at 100% efficacy after one single dose following a lethal challenge with the virus. The Company's production plant in Amsterdam has delivered clinical trial materials to the U.S. clinical trials are set to begin in the fourth quarter 2005.

West Nile virus. Crucell is developing a human vaccine against the West Nile virus. To date, the Company has conducted preclinical studies using geese, which are considered the best animal model for testing a potential West Nile virus vaccine. These initial tests successfully demonstrated disease-free survival in geese vaccinated with an experimental version of the Crucell vaccine following a lethal dose of the West Nile virus. Based on these results, the Kimron Veterinary Institute in Israel licensed PER.C6[®] technology to develop a veterinary vaccine, which has subsequently received market authorization. Crucell has the exclusive rights to market the PER.C6[®]-based West Nile virus veterinary vaccine in the United States.

- *Update.* Crucell has made significant progress with regard to growing the West Nile virus and has received Israeli market authorization for its veterinary vaccine developed with Kimron this past June. Crucell's Biosafety Level III Development Facility produced the material that was the basis of this authorization. In November 2004 it was announced that a contract had been signed with the Netherlands Vaccine Institute (NVI) to produce clinical trial material for the human vaccine trials.

Clinical trials of Crucell's human West Nile virus vaccine are set to begin during the fourth quarter of 2005

Malaria. Crucell announced at the end of October 2003 that it is developing a malaria vaccine in two collaborative programs involving three leading malaria research organizations: NYU, GlaxoSmithKline Biologicals, and WRAIR. The malaria vaccine candidate is based on Crucell's patented AdVac[®] adenovirus vector technology, and is produced using the Company's PER.C6[®] technology.

- *Update.* Crucell is currently conducting large animal studies, combining and comparing Crucell's and GlaxoSmithKline's vaccines. Crucell's own AdVac[®]-based vaccine showed excellent immune responses in monkeys. Crucell received a grant of up to €2 million from the SenterNovem Program of the Dutch Ministry of Economic Affairs in December 2004 to support its malaria research and AdVac[®] technology development. Clinical trials are set to begin in 2006.

Licensing Agreements for Technology

In addition to its internal development efforts described above, the Company continues to actively solicit and license its PER.C6[®] and AdVac[®] technologies to third parties. This strategy has increased the awareness and acceptance of the technology throughout the biopharmaceutical industry. Areas where Crucell is licensing the technology include vaccines, antibodies and therapeutic proteins, and gene therapy. Each of its licensees in these areas carries an annual payment, an upfront payment, and eventual royalty payments. The upfront payments vary from approximately €100,000 to €250,000, which are equal to the annual payments for contracts; royalties from 2% in gene therapy to 3-5% in antibodies; and up to low double digits in the field of vaccines.

Currently, Crucell has greater than three dozen licensees for its PER.C6[®] technology and growing. The popularity of the technology comes from its versatility and applicability to a wide range of human diseases. By increasing the number of third party licenses, the number of products derived from the technology may increase, resulting in the potential for additional licensing and royalty income. Table 2 (page 10) provides a snapshot of the Company's key licensees and partners, with some key descriptions below.

sanofi aventis SA. In December 2003, Crucell entered into a collaboration and license agreement with Aventis Pasteur to research, develop, manufacture, and market influenza vaccine products based on PER.C6[®] technology. This includes worldwide rights (except Japan). Under the terms of the agreement, Aventis Pasteur was granted an exclusive license in exchange for an up-front payment, milestone payments, annual payments, research and development funding, and royalties on future PER.C6[®]-based influenza vaccine sales. This includes milestone and upfront payments of up to €30 million, including up to €8 million upfront. Crucell could receive up to double digit royalties on the net sales of this product, with the idea being that the egg-based product will eventually be replaced by a cell-based product. Crucell believes that its technology is able to address the problems which have surfaced as of late with the current flu manufacturing processes.

Merck & Co., Inc. In October 2002, Crucell entered into an agreement with Merck & Company, in which Merck was granted an exclusive license to use Crucell's PER.C6[®] technology to develop vaccines for the prevention and treatment of HIV/AIDS. Currently in Phase II, clinical trials of the vaccine have seen the study expand to more than 1,000 people. Scientists hope that the trial leads to the development of a vaccine that would effectively prevent the development of AIDS from HIV infection, as well as treat the HIV infection in infected patients taking anti-retroviral therapy. Merck is implementing an extensively modified recombinant adenovirus that is grown using Crucell's PER.C6[®] technology. In October 2003, Crucell announced that Merck elected to extend its option for exclusivity to develop hepatitis C virus vaccines using the PER.C6[®] technology.

- *Update.* On December 15, Crucell announced that Merck had met a clinical development for milestone in connection with the PER.C6[®] technology licensed to Merck for its investigational HIV program.

Other Agreements. Crucell's extensive PER.C6[®] technology licensing program provides an ongoing revenue stream in the form of upfront payments and annual fees, and may provide future revenue in the form of royalties on product sales. More than three dozen pharmaceutical and biotechnology companies worldwide have selected Crucell's PER.C6[®] technology to develop their own products. Several of these products are in various stages of development including licensees such as Biogen Idec, Centocor/Johnson & Johnson (JNJ-NYSE), and GenVec (GNVC-NASDAQ).

AdVac[®] Technology

Apart from the PER.C6[®] technology, the Company has developed AdVac[®] technology—a different serotype of the common cold virus. The advantage of this technology is that most of the population has less naturally occurring immune responses against this technology, which means that it can be more efficacious for some of the diseases such as malaria, tuberculosis (TB), and HIV. Specifically, AdVac[®] technology is being applied by Crucell in the production of a malaria vaccine in collaboration with GlaxoSmithKline, Walter Reed Army Institute of Research, and the National Institute of Allergy and Infectious Diseases of the NIH, as well as a TB vaccine in collaboration with the Aeras Global TB Vaccine Foundation.

Also, Crucell and the International AIDS Vaccine Initiative (IAVI) have signed an exclusive license agreement to develop an AIDS vaccine where Crucell expects to receive development funding and substantial upfront, annual, and milestone payments, as well as royalties on future HIV vaccine sales. The AdVac[®] vectors, adenovirus serotypes 11 and 35, have shown promising results as vectors for AIDS vaccines in a series of studies by Crucell in collaboration with Harvard Medical School. These efforts could prove quite significant since, according to the World Health Organization (WHO), almost 5 million people became *newly infected* with HIV in 2003—the greatest number in any single year since the beginning of the epidemic. Globally, it is estimated that 38 million people are now living with HIV. More than 20 million people have died of AIDS since the first cases were identified.

Table 2
CruceLL N.V.

PER.C6[®] AND ADVAC[®] LICENSEE PIPELINE

Licensor/Partner	Technology Platform	Disease Target	Development Stage
Vaccines			
Aeras Global TB Vaccine Foundation	PER.C6 [®] & Advac [®]	Tuberculosis	Preclinical
Aventis Pasteur S.A.	PER.C6 [®]	Influenza	Preclinical
Chiron Corp.	PER.C6 [®]	Alphavirus vectors	Preclinical
Harvard School of Medicine	PER.C6 [®] & Advac [®]	Undisclosed	Preclinical
International AIDS Vaccine Initiative	Advac [®]	HIV	Preclinical
Kimron Veterinary Institute	PER.C6 [®]	West Nile virus – veterinary vaccine (avian)	Market authorization in Israel
MedImmune, Inc.	PER.C6 [®]	Influenza	Preclinical
Merck & Co., Inc.	PER.C6 [®]	Hepatitis C (option)	Preclinical
Merck & Co., Inc.	PER.C6 [®]	HIV	Phase II
Merial LLC	PER.C6 [®]	Foot and mouth disease	Preclinical
National Institutes of Health	PER.C6 [®] & Advac [®]	Ebola, Marburg and Lassa	Preclinical
National Institutes of Health	PER.C6 [®] & Advac [®]	Malaria	Preclinical
New York University	PER.C6 [®] & Advac [®]	Malaria	Preclinical
Vaxin, Inc.	PER.C6 [®]	Rabies	Preclinical
Vaxin, Inc.	PER.C6 [®]	Respiratory viruses	Preclinical
Walter Reed Army Institute of Research & GlaxoSmithKline Biologicals	PER.C6 [®] & Advac [®]	Malaria	Preclinical
Antibodies and Therapeutic Proteins			
AME, Inc./Eli Lilly	PER.C6 [®]	Portfolio	Phase I
Biogen Idec, Inc	PER.C6 [®]	Undisclosed	Preclinical
Centocor, Inc. (Johnson & Johnson)	PER.C6 [®]	Portfolio	Preclinical
Chiron Corp.	PER.C6 [®]	Portfolio	Preclinical
GlaxoSmithKline Ltd	PER.C6 [®]	Portfolio	Preclinical
Innogenetics	PER.C6 [®]	Portfolio	Preclinical
Merck & Co., Inc.	PER.C6 [®]	Portfolio	Preclinical
Merus B.V.	PER.C6 [®]	Portfolio	Preclinical
Micromet	PER.C6 [®]	Monoclonal antibody	Preclinical
Millipore	PER.C6 [®]	—	—
MorphoSys AG	PER.C6 [®]	Portfolio	Preclinical
PanGenetics	PER.C6 [®]	Portfolio	Preclinical
Synergenics/Synco Biopartners	PER.C6 [®]	Portfolio	Preclinical
Gene Therapy			
GeneMax Corp.	PER.C6 [®]	Portfolio	Preclinical
Edwards Lifesciences	PER.C6 [®]	Adenoviral vectors	Preclinical
EMD Lexigen Pharmaceuticals Corp. (Merck KgaA)	PER.C6 [®]	Portfolio	Preclinical
Eurogene Ltd (Ark Therapeutics)	PER.C6 [®]	Portfolio	Preclinical
GenVec Inc.	PER.C6 [®]	Cardiovascular product	Phase II
GlaxoSmithKline Ltd	PER.C6 [®]	Portfolio	Preclinical
Merck & Co., Inc.	PER.C6 [®]	Portfolio	Preclinical
ML Laboratories	PER.C6 [®]	Portfolio	Phase I/II
NeoTropiX	PER.C6 [®]	Oncology	Preclinical
Selective Genetics, Inc.	PER.C6 [®]	Portfolio	Phase I/II
Transgene SA	PER.C6 [®]	Portfolio	Phase I/II
Wyeth	PER.C6 [®]	Undisclosed	Preclinical
Genomics			
Galapagos Genomics	PER.C6 [®]	Genomics	

Source: CruceLL N.V.

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Crystal  Research
a s s o c i a t e s

Jeffrey J. Kraws or Karen B. Goldfarb
Phone: 212-201-6638
Fax: 212-838-4568
Email: eio@crystalra.com
Web: www.crystalra.com

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