

QUARTERLY UPDATE

First Quarter Financial Results Reported

Snapshot

May 10, 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).



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Recent Financial Data

Ticker (Exchange)	CRXL (NASDAQ)
Recent Price (05/10/05)	US\$19.83
52-Week Range	US\$6.55-20.44
Shares Outstanding (mm)	US\$36.9
Market Cap. (mm)	732.7
Average 3-month volume	176,400
Insider +5% Owners	>96%
Institutional Owners	40%
EPS (quarter ended 03/31/05)	(US\$0.18)
Employees	>200



Key Points

Euros (€) are converted to U.S. Dollars (US) at the March 31, 2005 exchange rate of 1.2916.

- Crucell N.V. reported financial results for first quarter 2005 on April 18. Revenue for the first quarter of €6.0 million (US\$7.7 million) represented an increase of 50% over revenue of €4.0 million (US\$5.2 million) for the corresponding quarter in 2004.
- Due to the increase in revenue, Crucell's net loss of €5.3 million (US\$6.8 million) for the first quarter 2005, represented a €0.14 net loss per share (US\$0.18) versus a net loss of €7.0 million (US\$9.1 million), or €0.19 net loss per share (US\$0.25) during the first quarter the year prior. A positive cash-flow of €177,000 (US\$229,000) for the quarter resulted in a cash balance of €76.9 million (US\$99.3 million) as of March 31, 2005.
- During the quarter, Crucell was granted a European patent for PER.C6[®] for vaccine production, and was granted other European and U.S. patents covering PER.C6[®] for protein production. New PER.C6[®] licensing agreements were concluded by the Crucell-DSM alliance with Roche, JCR Pharmaceuticals, and Mitsubishi. Crucell has also entered into additional PER.C6[®] arrangements with SingVax Pte. Ltd. of Singapore and Vascular Biogenics Ltd. of Israel.
- Crucell was further granted U.S. patent protection for its STAR[™] technology and Genentech Inc. (DNA-NYSE) began the second phase of its evaluation of STAR[™] technology's ability to improve the production yields of Genentech's proprietary systems.

Financial Results

Note: Euros (€) are converted to U.S. Dollars at the March 31, 2005 exchange rate of 1.2916.

First Quarter 2005

Crucell N.V. reported financial results for first quarter 2005 on April 18. Revenue for the first quarter of 2005 was €6.0 million (US\$7.7 million), representing an increase of 50% over revenue of €4.0 million (US\$5.2 million) for the corresponding quarter in 2004. License revenue for the quarter was €1.8 million (US\$2.4 million) versus €2.2 million (US\$2.8 million) for the first quarter of 2004. License revenue was comprised of initial payments from new contracts, in addition to annual payments, and other payments on existing contracts.

Service fees totaled €2.5 million (US\$3.2 million), representing a more than 300% increase over the €600,000 (US\$800,000) in service fees reported in the first quarter the year prior. Service fees are revenues for activities pursued under contract with partners and licensees. Service fee revenues increased during the first quarter 2005 as a result of the increased service activity in the influenza and malaria programs. Government grants and other revenues totaled €1.6 million (US\$2.1 million) versus €1.2 million (US\$1.5 million) during the first quarter 2004.

Total costs and expenses increased by 2.3% versus the same period of the preceding year. Total research and development (R&D) expenses for the first quarter 2005 was €5.9 million (US\$7.6 million), not including the cost of service fees, versus €6.1 million (US\$7.9 million) for the first quarter 2004. Selling, general, and administrative (SG&A) expenses for the first quarter 2005 totaled €2.7 million (US\$3.5 million) versus €4.1 million (US\$5.3 million) during the first quarter 2004. This reduction in SG&A expenses was caused by a reduction in warrant and non-employee stock option expenses, and other general and administrative expenses.

Due to the increase in revenue, Crucell's net loss of €5.3 million (US\$6.8 million) for the first quarter 2005, represented a €0.14 net loss per share (US\$0.18) versus a net loss of €7.0 million (US\$9.1 million), or €0.19 net loss per share (US\$0.25) during the first quarter the year prior.

Crucell's cash and cash equivalents on hand at the end of the first quarter 2005 was €76.9 million (US\$99.3 million), representing an increase of €200,000 (US\$258,000) over that of the first quarter 2004. Cash of €3.5 million (US\$4.6 million) was expended for operating activities during the first quarter this year. Net cash used in investing activities in the first quarter 2005, notably the purchase of equipment, totaled €300,000 (US\$387,000).

The Company's financing activities generated revenue of €4.0 million (US\$ 5.2 million) in the first quarter 2005 due largely to the proceeds of the issuance of ordinary shares after employee stock options were exercised during the period. The Company's management anticipates a full year cash burn of €15-20 million (US\$19-26 million).

Recent Events

- *On April 14, 2005, Crucell announced that it had signed a manufacturing contract with the Vaccine Research Center (VRC) of the National Institute of Allergy and Infectious Diseases (NIAID) which is part of the U.S. National Institutes of Health (NIH), for the manufacture of vaccines against Ebola infections. Under the terms of the contract, Crucell will manufacture as many as ten batches of clinical material of the PER.C6[®]-based Ebola vaccine in its own manufacturing facility. These materials will be used for Phase I and early Phase II clinical studies in humans. Crucell will receive up to €21.4 million (US\$27.6 million) from the VRC for the manufacture of the clinical lots.*
- *On April 5, 2005, Crucell announced that it had been granted a patent by the United States Patent and Trademark Office for its STAR[™] technology. The new patent is the first pertaining to the STAR[™] technology developed by professor Arie Otte of Chromagenics B.V., a company acquired by Crucell in March 2004, and covers the identification and selection of so-called STAR[™] sequences that are used for enhancing the production of therapeutic proteins in cell-culture systems.*
- *On April 1, 2005, Crucell announced that its partner sanofi pasteur, the vaccines business segment of the sanofi-aventis Group, had been awarded a US\$97 million contract by the U.S. Department of Health and Human Services (HHS) to accelerate the U.S. licensure of a PER.C6[®]-based cell-culture influenza vaccine and vaccine manufacturing facility. Crucell will be a subcontractor for the program. Terms of the subcontracting agreement between Crucell and sanofi pasteur were not disclosed. The project is part of the U.S. government's effort to increase domestic influenza vaccine manufacturing capacity in the event of a pandemic or other influenza health emergency. Within three years, Phase I and II clinical studies are expected to be completed, and a Phase III trial is expected to have commenced. Sanofi pasteur will also deliver to the HHS a feasibility plan for the construction of a U.S.-based and licensed cell-culture production plant for supplying up to 300 million monovalent influenza vaccine doses annually.*
- *On March 30, 2005, Crucell announced that it had signed a PER.C6[®] research license agreement with Israeli biopharmaceutical company Vascular Biogenics Ltd. The non-exclusive agreement will allow Vascular Biogenics to use the PER.C6[®] cell line for the preparation and evaluation of gene therapeutics based on adenoviral vectors. Under the terms of the agreement, Vascular Biogenics will make a research license payment and annual maintenance fees.*
- *On March 23, 2005, Crucell and allied contract manufacturer DSM Biologics announced that DSM Biologics had signed a PER.C6[®] research license agreement with the Japanese pharmaceutical company Mitsubishi Pharma Corporation. The license agreement enables Mitsubishi to use the PER.C6[®] cell line for production of certain recombinant therapeutic proteins. Under the terms of the agreement, Mitsubishi will make an upfront payment and pay annual maintenance fees.*
- *On March 22, 2005, Crucell announced the signing of a commercial PER.C6[®] license agreement with Singapore-based company SingVax Pte. Ltd. for the development and commercialization of new vaccines against Japanese encephalitis. Under the terms of the agreement, SingVax will focus on the development and commercialization of a Japanese encephalitis vaccine for the local population as well as for foreigners traveling to the Asia Pacific region. Crucell will receive upfront, annual and milestone payments under the agreement, as well as royalties on product sales. Crucell will also have a preferred position in the negotiation of marketing rights outside the Asia Pacific Region with respect to a traveler's vaccine that may be developed under the agreement in the event that SingVax makes such a product available for licensing.*
- *On March 18, 2005, Crucell announced that it had obtained an exclusive license to certain patents of the U.S. NIH to develop and commercialize recombinant vaccines against Ebola. The patents cover valuable vaccine components, such as the Ebola antigens and vectors. Additionally, the license covers 'one-shot' emergency vaccination strategies that have proven to be effective in relevant animal models.*

- *On March 17, 2005, Crucell announced that it had extended the Cooperative Research and Development Agreement (CRADA) with the Vaccine Research Center (VRC) for the development of vaccines to protect against Ebola, Marburg, and Lassa infections.* Under the existing CRADA, Crucell and the VRC have developed a PER.C6[®]-based Ebola vaccine which is undergoing pre-clinical evaluation. In the extended CRADA, Crucell and the VRC will continue to develop this vaccine and will use the Ebola vaccine results in the development of Marburg and Lassa vaccines. Under the terms of the agreement, the NIAID will provide funding for the experiments performed at the VRC and for animal studies, which will be performed at the U.S. Army Medical Research Institute of Infectious Diseases (USAMRIID). Crucell has the option for exclusive commercialization rights to any intellectual property generated by the VRC on the Ebola, Marburg, and Lassa vaccines that falls under the research plan of this CRADA. The vaccines could be useful as counter-measures against deliberate release of these infectious agents in bio-terror attacks.
- *On March 10, 2005, Crucell and allied contract manufacturer DSM Biologics announced that they had signed a PER.C6[®] research license agreement with JCR Pharmaceuticals Co., Ltd. of Japan.* This license agreement allows JCR to use the PER.C6[®] cell line for production of certain recombinant therapeutic proteins. Under the terms of the agreement, JCR will pay a research license payment, and pay annual maintenance fees.
- *On February 16, 2005, Crucell and allied contract manufacturer DSM Biologics announced that they had signed a PER.C6[®] research license agreement with Roche.* This license agreement allows Roche to use the PER.C6[®] cell line for production of monoclonal antibody products as well as a specific undisclosed protein. Roche has selected PER.C6[®] for this particular protein because it believes that PER.C6[®] possesses unique features capable of delivering the appropriate product quality. Further to this agreement, Crucell will work with Roche in creating a production clone for the specific protein. Under the terms of the agreement, Roche will pay a research license payment, annual maintenance fees, and research funding.

Crucell also announced on February 16 that it had been granted two pivotal patents relating to the production of proteins, one by the United States Patent and Trademark Office and the other by the European Patent Office. The U.S. Patent (No: 6,855,544) was granted on February 15, 2005, while the European patent (No: 1161548) was granted on February 16, 2005. With these two patents Crucell considerably strengthened its patent position in and around the manufacturing of monoclonal antibodies and therapeutic proteins using cell lines and production technology marketed under its trademark PER.C6[®].

- *On January 14, 2005, Crucell announced that it had been accepted as a member of the Influenza Vaccine Supply (IVS) international task force.* This specialized group within the International Federation of Pharmaceutical Manufacturers and Associations (IFPMA) was 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. The IVS member companies represent more than 90% of global influenza vaccine production, and are all involved in efforts to ensure production can meet the demands of a pandemic outbreak. Other members are Crucell's partner in its epidemic and pandemic flu vaccine programs, Sanofi Pasteur (formerly known as Aventis Pasteur), along with Sanofi Pasteur MSD, Baxter Vaccines (BAX-NYSE), Berna Biotech AG (BBITF.PK), Biken, Chiron Vaccines (CHIR-NASDAQ), CSL Ltd, Denka Seiken, GlaxoSmithKline Biologicals, ID BioMedical Corp. (IDBE-NASDAQ), Kaketsuken, Kitasati Institute, MedImmune Inc. (MEDI-NASDAQ), and Solvay Pharmaceuticals (SVYSF.PK-NASDAQ).
- *On January 7, 2005, Crucell announced that Genentech, Inc. would begin a second phase of evaluating Crucell's STAR[™] technology for the production of antibodies and other proteins.* In a joint evaluation program that is funded by Genentech, the two companies are investigating whether STAR[™] technology can increase the production yields of Genentech's proprietary systems. The first phase of the evaluation studied production yields in screening assays. Based on these results, Genentech has decided to enter into a second phase in which Genentech will test the effectiveness of STAR[™] under scaled-down production conditions. If the final phase of the evaluation proves successful, Genentech has an option to sign a non-exclusive STAR[™] license agreement, which will

be the first license for the STAR™ technology since Crucell's acquisition of ChromaGenics in March 2004.

- *On January 5, 2005, Crucell announced that it had been granted 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) 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.*

Corporate Growth Strategy

Crucell maintains a growth strategy of becoming 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.* 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. Crucell's cell culture technology has become part of a major U.S. government influenza pandemic vaccine program. Sanofi pasteur/Crucell is the only manufacturer in the European FLUPAN collaboration. Crucell was made a member of the Influenza Vaccine Supply (IVS) International Task Force.
- *Ebola.* Crucell announced that it had signed a manufacturing contract with the Vaccine Research Center (VRC), of the National Institute of Allergy and Infectious Diseases (NIAID) which is part of the U.S. National Institutes of Health (NIH), for the manufacture of vaccines against Ebola infections. Crucell also obtained an exclusive license to patents of the NIH to develop and commercialize vaccines against Ebola. Ebola, Marburg and Lassa viruses cause hemorrhagic fever, a highly lethal syndrome characterized by fever and bleeding. These viruses have been listed by the NIAID as category A priority agents, and as such are covered by the BioShield Act 2004, passed by the US Senate on May 19, 2004. BioShield is expected to appropriate US\$ 5.6 billion for the development of countermeasures against chemical and biological weapons.
- *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.

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 sanofi-aventis SA. 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, the sanofi-aventis Group 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.* On April 1, 2005, Crucell announced that its partner sanofi pasteur, the vaccines business segment of the sanofi-aventis Group, had been awarded a US\$97 million contract by the U.S. Department of Health and Human Services (HHS) to accelerate the U.S. licensure of a PER.C6[®]-based cell-culture influenza vaccine and vaccine manufacturing facility. Crucell will be a subcontractor for the program. Terms of the subcontracting agreement between Crucell and sanofi pasteur were not disclosed.

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.* On April 14, 2005, Crucell announced that it had signed a manufacturing contract with the Vaccine Research Center (VRC), of the National Institute of Allergy and Infectious Diseases (NIAID) which is part of the U.S. National Institutes of Health (NIH), for the manufacture of vaccines against Ebola infections. Under the terms of the contract, Crucell will manufacture as many as ten batches of clinical material of the PER.C6[®]-based Ebola vaccine in its own manufacturing facility.

Also, on March 18, 2005, Crucell announced that it had obtained an exclusive license to certain patents of the U.S. NIH to develop and commercialize recombinant vaccines against Ebola. The patents cover valuable vaccine components, such as the Ebola antigens and vectors. Additionally, the license covers 'one-shot' emergency vaccination strategies that have proven to be effective in relevant animal models.

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.

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.

Pipeline Summary

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 expected 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.

Licensing Agreements for Technology

In addition to its internal development efforts, 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 40 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.

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.

STAR[™] Technology

The STAR[™] technology, acquired in March 2004 from ChromaGenics B.V. (a privately held biotechnology company based in Amsterdam, the Netherlands) is focused on (epi) genetic discoveries relevant to recombinant DNA protein production in mammalian cells. STAR[™] elements are of particular importance to stable and 'high-yield' gene expression and are particularly useful for the production of recombinant human antibodies.

- *Update.* On April 5, 2005, Crucell announced that it had been granted a patent by the United States Patent and Trademark Office for its STAR[™] technology. The new patent is the first pertaining to the STAR[™] technology developed by professor Arie Otte of Chromagenics B.V., a company acquired by Crucell in March 2004, and covers the identification and selection of so-called STAR[™] sequences that are used for enhancing the production of therapeutic proteins in cell-culture systems.

Also, on January 7, 2005, Crucell announced that Genentech, Inc. would begin a second phase of evaluating Crucell's STAR[™] technology for the production of antibodies and other proteins. In a joint evaluation program that is funded by Genentech, the two companies are investigating whether STAR[™] technology can increase the production yields of Genentech's proprietary systems.

Table 2
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PER.C6® AND ADVAC® LICENSEE PIPELINE

Licensee/Partner	Technology Platform	Disease Target	Development Stage
Vaccines			
Aeras Global TB Vaccine Foundation	PER.C6® & Advac®	Tuberculosis	Preclinical
Chiron Corp.	PER.C6®	Alphavirus vectors	Preclinical
Harvard School of Medicine	PER.C6® & Advac®	SIV	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
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
sanofi-aventis	PER.C6®	Influenza	Preclinical
SingVax Pte Ltd	PER.C6®	Japanese encephalitis	Preclinical
Vaxin, Inc.	PER.C6®	Respiratory viruses	Preclinical
Walter Reed Army Institute of Research	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
Ferring Pharmaceuticals	PER.C6®	Women's health	Preclinical
GlaxoSmithKline Ltd	PER.C6®	Portfolio	Preclinical
Innogenetics	PER.C6®	Portfolio	Preclinical
JCR Pharmaceuticals Co. Ltd	PER.C6®	Undisclosed	Preclinical
Merck & Co., Inc.	PER.C6®	Portfolio	Preclinical
Merus B.V.	PER.C6®	Oligoclonics™ Portfolio	Preclinical
Micromet AG	PER.C6®	Portfolio	Preclinical
Millipore	PER.C6®	Undisclosed	Preclinical
Mitsubishi Pharma Corporation	PER.C6®	Undisclosed	Preclinical
MorphoSys AG	PER.C6®	Portfolio	Preclinical
PanGenetics	PER.C6®	Portfolio	Preclinical
Roche	PER.C6®	Undisclosed	Preclinical
Synergenics/Synco Biopartners	PER.C6®	Portfolio	Preclinical
Gene Therapy			
Edwards Lifesciences	PER.C6®	Portfolio	Preclinical
EMD Lexigen Pharmaceuticals Corp. (Merck KgaA)	PER.C6®	Portfolio	Preclinical
Eurogene Ltd (Ark Therapeutics)	PER.C6®	Portfolio	Preclinical
GeneMax Corp.	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
Vascular Biogenics Ltd	PER.C6®	Gene Therapeutics	Preclinical
Wyeth	PER.C6®	Undisclosed	Preclinical
Genomics			
Galapagos Genomics	PER.C6®	Genomics	

Source: CruceLL N.V.

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a s s o c i a t e s

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