



## **PRESS RELEASE**

### **Crucell Announces Positive Results of Phase II Clinical Study Rabies Monoclonal Antibody Combination in US**

#### ***Additional Milestone Achieved in Collaboration Agreement with sanofi pasteur***

**Leiden, The Netherlands, 1 October 2008** – Dutch biopharma company Crucell N.V. today announced the preliminary results of the first phase II clinical study of its investigational rabies monoclonal antibody combination, which started on 31 March 2008 in the US.

Crucell has a collaboration and commercialization agreement with sanofi pasteur, the vaccines division of sanofi-aventis Group, for Crucell's rabies monoclonal antibodies to be used in combination with rabies vaccine for post-exposure prophylaxis against this fatal disease.

The preliminary results of the US study were presented today by Dr. Christophe Python, at the XIX Rabies in the Americas RITA conference in Atlanta, U.S.

This phase II trial was set up as a randomized, single-blind, controlled study in 140 healthy volunteers and tested the antibody product in association with sanofi pasteur human diploid cell rabies vaccine. The study compared the rabies monoclonal antibody combination to a currently marketed human rabies immune globulin or placebo, in association with the rabies vaccine in a simulated rabies post-exposure setting.

A total of 140 subjects were randomized into the study, 80 in the CL184 monoclonal antibody combination treatment group, 40 in the human rabies immune globulin group and 20 in the placebo group. All subjects completed the study. There was no serious adverse event reported. Most adverse events were mild or moderate in severity. Overall, the systemic safety was comparable in the placebo, the HRIG and the monoclonal antibody combination groups. Injection site reactions to the monoclonal antibody combination, the human rabies immune globulin or placebo were reported by 12.5%, 65 % and 30% of the subjects, respectively.

The neutralizing activity against the rabies virus (a surrogate marker for protection) provided by the monoclonal antibody combination was comparable to that provided by the comparator. By day 14, all subjects administered the monoclonal antibodies combination together with the rabies vaccine reached the level of 0.5 IU/ml, a neutralizing activity levels thought to provide protection. Of note, the development of the immune response to the rabies vaccine was comparable in the monoclonal antibody combination and the human rabies immune globulin groups. These encouraging preliminary results are paving the way for the further development of this potentially life-saving medicine.



On February 12<sup>th</sup>, 2008 Crucell announced that its rabies monoclonal antibody combination was granted Fast Track status by the US Food and Drug Administration (FDA). A second phase II clinical study started on May 13, 2008, in the Philippines, and is expected to be completed before year-end 2008. The trial, which is being carried out in 48 healthy adolescents and children, aims to generate safety data in these populations.

"We are very pleased with our continued and rapid progress with this next generation rabies treatment," said Ronald Brus, Crucell's Chief Executive Officer. "These results and the milestone achieved put us another step closer to our ambition of reducing the global burden of this fatal disease."

#### **About 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 encephalitis (inflammation of the brain) and ultimately death if medical intervention is not sought promptly after exposure. There is no proven treatment for rabies once symptoms of this fatal disease have appeared. Rabies is prevented by post-exposure prophylaxis (PEP) with the combined administration of a rabies vaccine and rabies immunoglobulin (RIG). Rabies is prevalent in Europe, Asia, Africa, North America and South America. Every year approximately 10 million people are vaccinated against the disease worldwide. An estimated 40,000 to 70,000 people die from rabies each year, mainly in Asia.

#### **About Crucell's rabies monoclonal antibody program**

Crucell's rabies monoclonal antibody product is a combination of two human monoclonal antibodies, generated using Crucell's MAbstract<sup>®</sup> technology and produced using Crucell's PER.C6<sup>®</sup> technology. Crucell's rabies monoclonal antibody combination offers the potential to replace the traditional serum-derived products that are currently used for rabies post-exposure prophylaxis. Phase I clinical trials data conducted in the United States and India supported further clinical development. The program has been granted a Fast Track designation by the Food and Drug Administration's (FDA) Department of Health and Human Services. The Fast Track program facilitates the development and expedites the review of new drugs that are intended to treat serious or life-threatening diseases and that demonstrate the potential to address unmet medical needs.

In December 2007, Crucell and sanofi pasteur signed an exclusive collaboration and commercialization agreement for Crucell's rabies monoclonal antibodies, next-generation rabies biologicals, to be used with rabies vaccine for post-exposure prophylaxis against this fatal disease. Under the terms of the agreement, Crucell will continue to perform the development activities. Crucell will be responsible for the manufacturing of the final product and will retain exclusive distribution rights in Europe, co-exclusive distribution rights in China and the rights to sell to supranational organizations such as UNICEF. Crucell received an initial payment of €10 million following the execution of the agreement and will be eligible for milestone payments of up to €66.5 million.

Peak sales for Crucell's rabies antibody combination are expected to exceed \$ 300 million.



#### **About PER.C6<sup>®</sup> technology**

Crucell's PER.C6<sup>®</sup> technology is a cell line developed for the large-scale manufacture of biopharmaceutical products such as recombinant proteins including monoclonal antibodies. The strengths of the PER.C6<sup>®</sup> technology lie in its safety profile, scalability and productivity under serum-free culture conditions.

#### **About MAbstract<sup>®</sup> technology**

Crucell's proprietary MAbstract<sup>®</sup> technology can be used to discover drug targets, such as cancer markers or proteins from infectious agents including bacteria and viruses, and identify human antibodies against those drug targets.

#### **About Crucell**

Crucell N.V. (Euronext, NASDAQ: CRXL; Swiss Exchange: CRX) is a global biotechnology company focused on research, development, production and marketing of vaccines, proteins and antibodies that prevent and treat primarily infectious diseases. Its vaccines are sold in public and private markets worldwide. Crucell's core portfolio includes a vaccine against hepatitis B, a fully-liquid vaccine against five important childhood diseases and a virosome-adjuvanted vaccine against influenza. Crucell also markets travel vaccines, such as the only oral anti-typhoid vaccine, an oral cholera vaccine and the only aluminum-free hepatitis A vaccine on the market. The Company has a broad development pipeline, with several product candidates based on its unique PER.C6<sup>®</sup> production technology. The Company licenses its PER.C6<sup>®</sup> technology and other technologies to the biopharmaceutical industry. Important partners and licensees include DSM Biologics, sanofi-aventis, Novartis, Wyeth and Merck & Co. Crucell is headquartered in Leiden, the Netherlands, with subsidiaries in Switzerland, Spain, Portugal, Italy, Sweden, Korea and the US. The Company employs over a 1000 people. For more information, please visit [www.crucell.com](http://www.crucell.com).

#### **Forward-looking statements**

*This press release contains forward-looking statements that involve inherent risks and uncertainties. We have identified certain important factors that may cause actual results to differ materially from those contained in such forward-looking statements. For information relating to these factors please refer to our Form 20-F, as filed with the U.S. Securities and Exchange Commission on June 13, 2007, and the section entitled "Risk Factors". The Company prepares its financial statements under generally accepted accounting principles in the United States (US GAAP) and Europe (IFRS).*

#### **For further information please contact:**

Oya Yavuz  
Director Corporate Communications & Investor Relations  
Tel: +31-(0)71-519 7064  
[ir@crucell.com](mailto:ir@crucell.com)