



## **CRUCCELL PRESENTS ADVAC™, A NEW IMPROVED VACCINE TECHNOLOGY**

*Improving the Gene Delivery Technology for Vaccination*

**Leiden, The Netherlands, June 1, 2001-** Crucell N.V. (NASDAQ: CRXL, Euronext Amsterdam: CRXL) today presents data demonstrating that their new system for vaccination, called AdVac™, stimulates a stronger immune response, with improved safety. The data will be presented today at the 4th annual meeting of the American Society for Gene Therapy (ASGT) in Seattle, Washington.

As part of its vaccine development program, Crucell has developed a new gene delivery system for vaccination purposes that better stimulates an immune response.

Current gene delivery systems (vectors) are derived from human adenovirus serotype 5, a common human common cold virus. These vectors need to be administered in high doses, because they poorly transduce the key target cells that elicit immune responses. Moreover, most people have been exposed to this type of adenovirus. As a result, current adeno-vaccines are very rapidly inactivated by the anti-adenovirus antibodies present in these individuals.

Crucell's new delivery system, AdVac™, is based on another type of adenovirus (serotype 35). The data presented today by Crucell show that the new AdVac™ vector in fact efficiently binds to and transduces cells that elicit a strong immune response. Furthermore, in contrast to the currently used vectors, the AdVac™ vector is not inactivated by the anti-adenovirus antibodies that are present in the majority of individuals. Finally, the vector does not infect liver cells, which is an unwanted side effect of currently used vectors.

As a consequence, Crucell expects that AdVac™-based vaccines will result in strong immune responses, while using a 100-fold lower dose compared to current adeno-vaccines, improving overall safety and efficacy of the vaccines.

AdVac™ forms a further improvement of Crucell's PER.C6™ technology for vaccines. Crucell applies its PER.C6™ cell line for the development of its influenza vaccine. Furthermore, PER.C6™ is currently used in clinical development by a number of pharmaceutical and biotech companies, including Merck & Co., Inc. who are using the PER.C6™ technology in their HIV-1 vaccines research program.



### **About AdVac™**

The new vectors were molecularly engineered from the adenovirus type 35, a serotype shown by Crucell scientists to bind effectively to human antigen presenting cells and skeletal muscle cells. Moreover, the vector is not inactivated by the anti-adenovirus antibodies that exist in the majority of individuals. The latter was tested using blood samples collected from more than 500 individuals in the US, Europe and Japan. An additional benefit of the adenovirus type 35-derived vectors is their dramatically reduced affinity for human liver cells. As the liver is very sensitive to current adenovirus type 5 vectors, this constitutes an important added safety feature.

### **About Crucell**

Crucell is a leading biotechnology company focused on the development of huMADE™ biopharmaceuticals such as human antibody-based therapeutics for treatment of cancer, inflammatory diseases and vaccines for the prevention and treatment of influenza and other infectious diseases, and on the discovery of unique drug targets on diseased cells.

Crucell's two broadly applicable human technology platforms form the basis for this. The first is a human cell line expression platform, PER.C6™, on which a wide range of biopharmaceuticals can be developed and manufactured, such as vaccines, antibodies, therapeutic proteins and gene therapy products. The second technology is called MAbstract™, a set of tools based on phage antibody-display libraries and proprietary subtraction and selection technology, to discover novel drug targets and develop human monoclonal antibodies as therapeutics for a variety of diseases. Biopharmaceuticals produced on Crucell's human PER.C6™ technology are called huMADE™.

Crucell makes its technologies available under exclusive or non-exclusive license agreements, and has currently signed 16 agreements with major pharmaceutical and biotechnology companies for its PER.C6™ technology.

Crucell has signed an exclusive agreement with Merck & Co., Inc. under which it was granted a license to use Crucell's PER.C6™ platform to develop vaccines for the prevention and treatment of HIV. This agreement also provides Merck the option of extending the exclusivity to cover three additional diseases in the future.

Crucell currently employs approximately 130 people in its facilities in Leiden and Utrecht.

**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. See our Registration Statement, as filed on Form F-1 with the U.S. Securities and Exchange Commission on October 26, 2000, (the "Registration Statement") and the section of the Registration Statement entitled "Risk Factors."**



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