

Company Overview

The company

Glycostem is a clinical stage biotech company established in the Netherlands in 2007. The company's headquarters and new state-of-the-art lab and production facilities are based at Pivot Park life sciences park in the Dutch city of Oss. The name 'Glycostem' was conceived to reflect the role of Glycosaminoglycans in stem cell growth and proliferation.

Glycostem has developed the world's first GMP-compliant platform technology enabling the generation of Natural Killer cells (NK-cells) from umbilical cord blood stem cells. NK-cells arise from blood-forming stem cells and are an essential part of the innate immune system. In 2017, Glycostem published a phase I trial with its cultured NK-cells (oNKord®) applied to the treatment of poor prognosis AML patients. This study demonstrated an excellent safety profile and positive initial efficacy data.

Therapeutic strategy

oNKord® is the first allogeneic NK-cell-based therapy ready for industrial scale-up. Around 5-10% of the lymphocytes (white blood cells) in the human body are NK-cells. NK-cells possess a broad spectrum of immune functions and their activity is regulated by a well-described set of activating and inhibitory receptors. NK-cell activation is balanced between activating and inhibitory cellular signals. A NK-cell will recognise and kill a target, once the activating signal is higher than the inhibitory signal. These mechanisms enable NK-cells to control viral infections and to target and kill cancer and senescent cells.

NK-cells provide the body with an enhanced immune rescue solution. By supplementing AML patients with ex vivo generated NK-cells, after intensive anti-cancer treatment, residual diseased cells may be eliminated. NK-cells may be employed both as a standalone and add-on therapy, thus allowing multiple treatment options.

-more-

Contact:

Troels Jordansen +31 6 1834 5326 - Troels@Glycostem.com – www.Glycostem.com

Glycostem is planning more clinical trials for 2019. One trial will see oNKord® tested as an add-on therapy (in relapsed and refractory AML patients). In a second trial oNKord® will be tested in Multiple Myeloma. There are also plans for entering solid tumour trials.

While NK-cells are expected to be deployed to numerous fronts in the battle against various diseases, Glycostem is focusing solely on oncology (cancer) indications. 1st generation NK-cells (as they are found in the body) are expected to be active in most haematological (blood) or defuse (early stage or post cancer surgery) cancers.

Lead product

Glycostem's primary objective is to validate oNKord® as a first-in-class therapy for AML patients. To this end, Glycostem is currently optimising production processes and carrying out the clinical development programs requisite for regulatory approval. In the long-term, with the goal of establishing the company as the preferred partner for development and production of therapeutic NK-cells, Glycostem aims to expand its current pipeline to other NK-cell-based therapies.

Technology and IP

The therapeutic potential of NK-cells is clear and evident, but clinical applications to date were limited by production issues such as low cell numbers, low activation status and the presence of residual cells. Glycostem has developed proprietary culturing methods to overcome these hurdles.

Brief explanation: Stem cells (CD34+) are isolated from the human umbilical cord and differentiated into NK-cells in a fully closed and automated cell culture system. Glycostem's proprietary methods produce an unprecedented quality of NK-cell cultures, in terms of cell count, activity and purity. Glycostem established a portfolio of six (6) patent families protecting its technologies. Importantly, the allogenic nature of oNKord® may constitute the world's first *off-the-shelf* cellular immunotherapy product.

Contact:

Troels Jordansen +31 6 1834 5326 - Troels@Glycostem.com – www.Glycostem.com

Target markets

The number of AML patients in the eight main target markets (top six in EU, US, and Japan) in 2020 is estimated at 130,000. Within this target market Glycostem anticipates the market share to expand to 2% over five years after market introduction. Accordingly, Glycostem expects to treat nearly 4,000 patients in the eight major markets within five years after market approval of oNKord®. Resulting revenue is expected to surpass €730 million.

Commercial strategy

Glycostem has obtained Orphan Drug Designation for AML in Europe and the USA.

Glycostem will leverage the results of its preclinical research, scale-up production, secure a sustainable supply chain and perform all clinical studies required by regulatory authorities to commercialise oNKord® as a therapeutic for AML. Upon completion of the phase II studies, Glycostem's strategy is to partner with a pharmaceutical company to facilitate successful commercialisation and the rapid global application of oNKord®. Should partnering progress not meet expectations in terms of rapidity and scope of expansion, Glycostem will establish its own sales and marketing operations in key markets.

Overcoming obstacles with state-of-the-art processes

Current cancer treatments, chemical and biological-based products, do not remedy fundamental complications. Such treatments:

- Work only temporarily, with a high rate of relapse;
- Often result in instances of resistance after repeated treatments;
- Result in patient immune system dysfunctionality;
- Intrinsically complicate combinatorial therapies.

Similarly, a clinical breakthrough in cellular therapy remains hampered and limited by myriad conditions:

- Most cell products are autologous, patient specific, incur excessive costs and processes must confront a range of logistical hurdles;

Contact:

Troels Jordansen +31 6 1834 5326 - Troels@Glycostem.com – www.Glycostem.com

- Based on individual product preparations, efficient large-scale production platforms cannot be established; and
- NK-cell therapy to date is limited by low cell numbers, low activation status and presence of residual T- and B-cells, with inherent risk of clinical complications.

To realize the blockbuster potential of NK-cell therapy, Glycostem developed the world's first stem cell derived, allogeneic NK-cell immunotherapy - oNKord®. Glycostem's therapeutic approach includes:

- Unlimited Sourcing – oNKord® is generated from hematopoietic stem cells.
- Universal Donor – oNKord® can be used across HLA-barriers as the absence of T-cells and B-cells limit the risk of clinical complications. The universal donor principle enables *off-the-shelf* products.
- Unrestricted Use – oNKord® targets several types of haematological or solid tumours.
- Future Proof – NK-cells offer the most flexible starting point for future NK-cells products as CAR-NK-cells, which likely will be genetically modified.

Proprietary culturing technologies

Glycostem's cell culturing technologies represent a watershed breakthrough in the generation of NK-cells for therapeutic purposes, given the high expansion potential of the system, combined with the high purity and functionality of the final product.

Glycostem has over the last decade focused on R&D to generate protocols for the optimal selection of CD34+ stem and progenitor cells from cryopreserved, or fresh umbilical cord blood (UCB). Similarly, Glycostem designed a closed cell culture process using a bioreactor system to generate large numbers of NK-cells. Interestingly, oNKord® displayed a gene expression profile similar to the cytolytic molecules, while cytotoxicity studies revealed that they also exert a significantly stronger killing ability compared to activated NK-cells from peripheral blood.

Contact:

Troels Jordansen +31 6 1834 5326 - Troels@Glycostem.com – www.Glycostem.com

The current system produces unprecedented high numbers of pure NK-cells. Up to 10 billion per batch surpass 90% purity and are devoid of contaminating T- and B-cells.

-end-

Contact:

Troels Jordansen +31 6 1834 5326 - Troels@Glycostem.com – www.Glycostem.com