



Taking cellular immunotherapy to the next level

Glycostem plans phase II trial start in early 2023 with off-the-shelf un-manipulated NK cells in AML

May 2022

Pioneering, developing and manufacturing

Glycostem is focused on the development of first-, second- and third-generation stem cell-derived Natural Killer cells (NK cells) as a therapeutic asset in the fight against cancer. In 2020 Glycostem started with the first-of-its-kind pivotal phase I/IIa trial in acute myeloid leukemia (AML) with in-house manufactured non-modified NK cells (oNKord[®]) and the first patient was dosed in December 2020. This is the first off-the-shelf immuno-oncology product to head for product approval worldwide and the first of a series of trials to follow.

NK cells are the new star in the domain of cellular immunotherapy, due to their tightly regulated 'natural killing' of cancer cells and the fact that no serious side

effects or complications arise from their use. They play an important role in control and even cure of both solid and hematological malignancies and thus have the potential to impact the lives and future of many cancer patients and their families. Over the last decade Glycostem has extensively studied the role of NK cells in cancer treatment and pioneered, developed and optimized its in-house NK cell production processes and products to the fullest. A growing number of commercial and academic partners have chosen Glycostem because of their expertise on NK cells and their production.

oNKord® - non-manipulated NK cells

oNKord® is Glycostem’s first generation allogenic NK cell therapy for hematological indications and solid tumors. Based on umbilical cord blood (UCB) derived CD34+ stem cells oNKord® has many advantages, like:

- oNKord® is allogenic and **off-the-shelf**, readily available with minimum waiting time
- **Safe:** since oNKord® does not cause Cytokine Release Syndrome (CRS) and feeder cells are not required
- **Cost-effective:** thanks to optimized Cytotoxicity (less cells are needed) and a closed in-house manufacturing system in batches

Next generations - CAR-NK and TCR-NK cells

Chimeric Antigen Receptor (CAR)-engineered NK cells are today one of the most attractive and innovative pre-clinical candidates in cellular immunotherapy because of their dedicated functionality, tumor targeting, prolonged persistence and fewer side effects compared to current CAR-T treatments. Having invested in the non-manipulated NK cells Glycostem has a wealth of information and experience leading up to this second-generation product.

Closed system transduction, two in-licensed and highly interesting and specific targets are the building blocks to releasing pre-clinical data late-2021 are on target. Glycostem is also researching T-cell receptor expression on NK cells for which proof of feasibility is available.

GMP licensed manufacturing platform

Our proprietary processes and closed in-house production system for allogeneic cellular products allows us to select and significantly increase the number of NK and CAR-NK cells (up to 50,000-fold in one production run from starting material) without the need for feeder cells. Glycostem obtained its GMP license in June 2019 and received the certificated in inspection November 2021.

Glycostem has invested many resources to achieve:

- Feeder-cell free cell expansion process; easier regulatory approval process saving time and quicker access to treatment for patients
- Closed system; contamination physically impossible and operating a very cost-effective level (class C/D vs open system class A/B)

- A manufacturing system for non-manipulated and manipulated NK cells; high synergy at cost effective levels
- Ongoing upscaling of our manufacturing process allowing a significant increase of the number of patients to be treated from one unit of umbilical cord blood (UCB)

1 unit of UCB	Cell yield	oNKord® 3 billion NK cells per treatment	CAR-NK 600 million CAR-NK cells per treatment
Now	20 to 25 billion NK cells	5 to 8 patients	20 to 25 patients
2 years' time	60 to 75 billion NK cells	15 to 24 patients	60 to 75 patients



Clinical strategy

Glycostem initiated oNKord® clinical trial in AML (WiNK study) patient in December 2020. The trial will take place in 5 European countries with the possible addition of a US trial center for the pivotal part of the trial.

After pre-IND discussions with the FDA, Glycostem is fully aware of the minor changes between European and US regulations.

As a next step, we are focusing on the development of our unique CAR-NK products, and preparing for pre-clinical testing. We expect to initiate phase I trials by early 2023. As a third-generation product Glycostem is working on TCR-NK products which may be around one year after the phase I CAR-NK trial. Above sequence is finely timed allowing Glycostem to develop increasingly complex forms of cancer treatment while building operational experience and conducting the data necessary for worldwide submissions.

Pipeline

Therapy	Product	Indication	Cell	Development	Pre-clinical	Phase I	Phase II	Phase III	Market Introduction	Partner
oNKord®	GTA002	AML / MM	NK cell	[Progress bar spanning Development, Pre-clinical, and Phase I]					2024	JP: inno.N; KR: inno.N
		Solid Tumors		[Progress bar spanning Development and Pre-clinical]						Glycostem
viveNK™	GTA102	Colon cancer	CAR-NK	[Progress bar spanning Development and Pre-clinical]					TBA	Glycostem
	GTA103	Glioblastoma		[Progress bar spanning Development and Pre-clinical]				inno.N		
	GTA104	Other solid tumors		[Progress bar spanning Development and Pre-clinical]				inno.N		
	GTA201	N/D	TCR-NK	[Progress bar spanning Development]				Glycostem		

Management

Our organization is guided by a highly experienced and specialized Management Team and supported by a Advisory Board that includes renowned experts in the field of innovative cancer therapeutics.



Troels Jordansen, CEO

20+ years' experience with cellular therapies and public listed company management



Jan Spanholtz, PhD, CSO

15+ years' background in stem cell biology, immunology, translational research and process development



Volker Huppert, Dipl.-Ing., CDO

20+ years of NK cell and closed system manufacturing experience



Kai Pinkernell, MD, CMO

20+ years of experience in the development of cell and gene therapies



Hans Henskens, PhD, CQO/QP

15+ years of experiences in pharmaceutical and cellular therapy with quality and manufacturing

Finance

Glycostem is funded up to and including the WiNK trial. Over the last 3 years Glycostem has raised more than \$35 million in equity, deal funding and soft government loans.

IP

Thanks to its nine patent families, long-standing technical expertise and resources, as well as Orphan Drug Designation, Glycostem has secured a leadership position in the global NK cell market.

Press release

13th May 2022

Glycostem announces new data presentation at EHA 2022 Congress highlighting early safety and clinical course of oNKord® in patients with Acute Myeloid Leukemia

4th November 2021

Glycostem announces initial clinical data to be presented at 2021 ASH Annual Meeting

12th Mar '21

Glycostem enters into MTA with Pieris to enhance solid tumor targeting capabilities of oNKord® and CAR-NK

17th Dec '20

Glycostem and Ghent University sign license agreement on NK cell therapy technology

15th Dec '20

First patient treated in phase I/IIa oNKord® trial for AML

3rd June '20

Glycostem digitizes its manufacturing process

12th Sep '19

Glycostem signs global CAR-NK product co-development deal

11th Sep '19

Glycostem out-license oNKord® for Korea and Japan

25th June '19

Glycostem receives GMP license

Glycostem Therapeutics B.V.

Kloosterstraat 9, 5349 AB Oss
The Netherlands

W: www.Glycostem.com

E: info@Glycostem.com