



**FOR IMMEDIATE RELEASE**

**GLYCOFI ANNOUNCES THE FIRST PRODUCTION OF ANTIBODIES WITH HUMAN GLYCOSYLATION IN YEAST.**

Publication in February issue of *Nature Biotechnology* Shows Potential to Design and Produce Antibodies with Improved Cell Killing, and Other Drug Characteristics in a Well Established Production System

**Lebanon, NH, January 23, 2005** -- Researchers at GlycoFi and Dartmouth College have reported the first production of monoclonal antibodies with human sugar structures in yeast. This research, published online January 22 and in the February issue of the journal *Nature Biotechnology*, demonstrates that antibodies with human sugar structures (glycosylation) can be produced in glyco-engineered yeast cell lines, and that by controlling the sugar structures of antibodies, their therapeutic potency can be significantly improved. Moreover, this same approach offers the potential to improve other glycosylation-dependent drug properties (such as solubility, half-life, or tissue distribution). Given the mature and well-established nature of yeast-based protein production technology, the reported work also promises to improve the production and scale-up economics of antibody manufacturing.

Monoclonal antibodies constitute the majority of therapeutic proteins currently in clinical and preclinical development, and additionally represent some of the largest selling products to emerge from the biotechnology industry. Monoclonal antibodies often achieve their therapeutic benefit through two binding events: 1) the binding of the variable domain of the antibody to a specific marker protein, such as the CD20 receptor on the surface of cancer cells, followed by 2) the recruitment of immune system “effector” cells that bind the constant domain of the antibody and destroy the cancer cell to which the antibody is bound. Research has shown that this process, known as antibody dependent cell cytotoxicity (ADCC), is sensitive to the composition of sugars (or “glycans”) in the antibody’s constant region. Moreover, in the absence of these sugars, the antibodies can bind to antigens but do not elicit ADCC.

“Mammalian cell cultures currently used for most therapeutic protein production produce a mixture of glycoforms and typically do not allow for the control of glycosylation,” said Tillman Gerngross, chief scientific officer of GlycoFi, and professor of Bioengineering at

Dartmouth College. “We have spent the last five years engineering yeast cell lines that perform human glycosylation, which now allows us to glycosylate proteins with unprecedented control and uniformity.”

In the study described in *Nature Biotechnology*, the researchers used several glyco-engineered yeast cell lines to produce a library of glycoforms of the anti-CD20 antibody rituximab and to compare their receptor binding properties to the mammalian-derived commercial counterpart, Rituxan®. The polypeptide backbone of each of the antibody variants produced in the GlycoFi yeast remained identical and only the glycosylation structures of each antibody was altered. Comparisons of the antibody variants with Rituxan® showed that antibody binding varied with changes in the glycosylation structure. Moreover certain antibody glycoforms showed significantly increased antibody mediated cell killing compared to Rituxan®.

“By controlling the sugar structures on antibodies we have shown that the antibodies ability to kill cancer cells can be significantly improved and that therapeutic proteins can be optimized by controlling their sugar structures,” says Dr. Huijuan Li, associate director of Analytical Development at GlycoFi, and the lead author of the study. She noted that while the current report focuses on antibodies, the approach taken by the GlycoFi team can be applied to any therapeutic glycoprotein. Moreover, in addition to cell killing, this approach can be applied to optimize other protein characteristics such as solubility, therapeutic half-life, tissue distribution and interaction with complement proteins. Currently glycoproteins comprise about 70% of all approved therapeutic proteins and the therapeutic protein market is expected to grow at over 20% annually over the next decade.

GlycoFi is now working to expand its library of glyco-engineered yeast cell lines and expects to obtain a large array of specific glycoprotein variants that were hitherto unobtainable at a commercial scale. The company believes that as the scale-up and recombinant production of proteins in yeast is a well established technology, more easily achieved than mammalian cell culture, it should be possible to produce specific designer glycoproteins at large scale using the company’s engineered yeasts. GlycoFi has already announced several major collaborations aimed at applying its technology to the production of specific therapeutic proteins, including collaborations with Merck, Eli Lilly and others.

### **About GlycoFi**

GlycoFi, Inc. is a private, venture-backed biotechnology company that has developed a novel, yeast-based, proprietary protein optimization technology that the company uses to develop, produce and commercialize Next Generation Biotherapeutics™, alone and in partnership with other leading biopharmaceutical companies. For additional information please visit [www.glycofi.com](http://www.glycofi.com).

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