



# GlycoForm

Michael Short

Corporate Presentation

Series 'A' Fund Raising

**Novel Synthetic  
Glycoproteins**

## Leading technology platform

- World-class expertise in complex sugar synthesis and chemical ligation processes
- Production of glycoproteins with homogeneous sugar content to deliver novel synthetic glycoprotein drugs optimised for efficacy, safety and efficiency
- Strong IP position
- Lead programme with animal efficacy shown in anaemia indication

## Multibillion dollar market

- Over \$24 billion annual sales (2005) from current glycoprotein products
- Outstanding opportunities to create improved next-generation products

## Clear exit options in reasonable timeframe

- Trade sale likely as recently proven for other glycoengineering companies

## **GlycoForm is raising £5 million to be used over the next 2 years to:**

- Advance its first programme to preclinical stage (first year), positioning it for partnering during the second year
- Expand the in-house development programme to include additional next-generation products
- Build collaborative ventures in fragments and peptides similar to that developed in monoclonal antibodies with Cambridge Antibody Technology

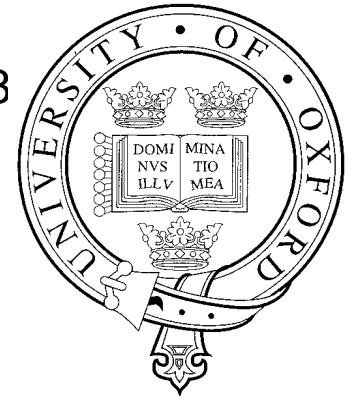
**Founded from the Chemistry Research Laboratory, University of Oxford, on world-leading expertise in the synthesis and conjugation of oligosaccharides to create next generation glycoproteins**

Professor Ben Davis, Founder

- Top 100 Young Innovator by *MIT Technology Review*, 2003
- Royal Society Corday-Morgan Medal, 2005

Dr Antony Fairbanks, Founder

- Royal Society of Chemistry Carbohydrate Award, 2004



International Scientific Advisory Board

Significant input from other industrial, commercial and academic experts

# Strong Intellectual Property



Patent	Technology	Priority Date
PCT/GB04/002706	GlycoSeS - Disulfide coupling technology	24 June 2003
PCT/GB2006/001274	GlycoClick - Coupling via non-natural amino acids	8 April 2005
UK 0517077.4	Glycolmage - Imaging agents using sugar targeting	19 August 2005
UK 0602352.7	Decasaccharide synthesis / disulfide coupling	6 February 2006

# Experienced Management Team



## **Michael Short, CEO**

- 23 years biotech and pharma experience at Bayer, Baxter and PathoGenesis (Chiron)
- Founder and CEO of Iridia and RioTech Pharmaceuticals

## **Chris Urch PhD, Head of Research**

- 26 years experience in synthetic organic chemistry at ICI/Zeneca and Amura

## **Alan Boyd MD, Head of Development (Consultant)**

- 25 years in medicine and drug development at Glaxo, ICI/Zeneca and Ark Therapeutics

## **Mario Polywka DPhil, CChem FRSC, Chairman**

- 16 years experience founding and running biotech companies
- Currently Chief Operating Officer, Evotec AG

## Protein glycosylation

- Up to 70% of all proteins in humans are glycosylated
- Glycosylation affects many aspects of glycoprotein function
  - antibody-dependent cell-mediated cytotoxicity
  - solubility, half-life and aggregation
- Proven technology in blockbuster drugs



- Therapeutic glycoprotein production is mainly in mammalian cell culture, an expensive and difficult procedure
- Current glycoprotein production is problematic and it creates batch-to-batch variability that challenge manufacturing, regulatory and clinical requirements

## Therapeutic optimisation

- Optimisation to a single glycoform that maximizes therapeutic performance and pharmaceutical properties

## Design flexibility

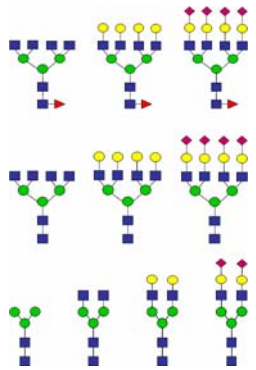
- Synthetic chemistry allows the production of any carbohydrate (natural and non-natural) at high purity, and the ability to make precise modifications allows SAR development

## Manufacturing advantages

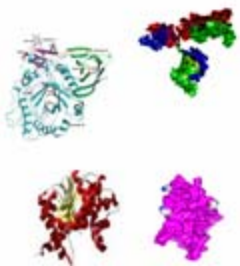
- Allows the use of the optimal low cost protein expression system
- Precise batch characterization

## Defined commercial opportunity

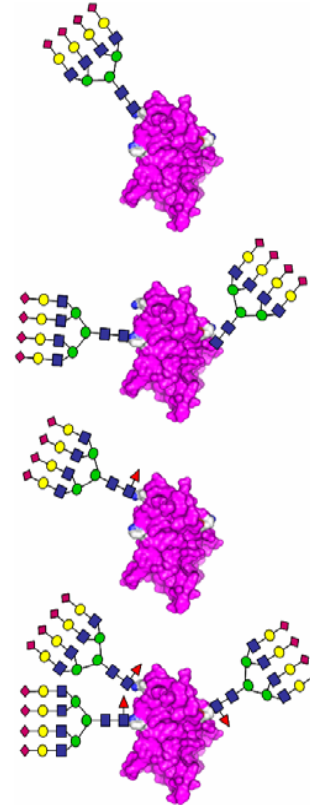
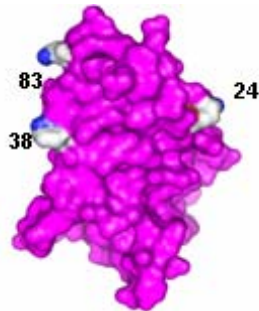
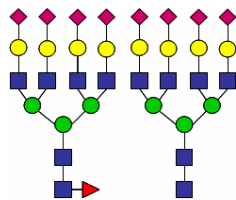
- Improve existing blockbuster therapies for life cycle management in known markets thereby reducing risk
- Enable new products (e.g. synthetic glycopeptides)
- Novel technology and advantage supports substantial collaborative deals



*Identify potential sugars from synthetic panel*

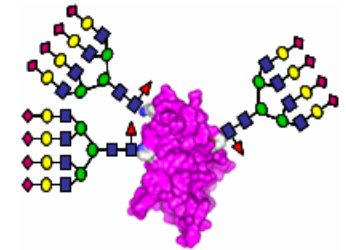


*Make proteins with cysteines as glycosylation sites in high yield system*



*Use GlycoSeS to site-specifically glycosylate  
Use GlycoExtend to introduce additional sugars*

*Novel Synthetic Glycoprotein*



Homogeneous product  
Number and position of glycans optimised for therapeutic effect  
Patented novel compound

## GlycoForm glycosylates through a precise process


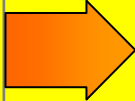
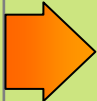
Target protein is made with free cysteine thiol(s) then

**GlycoSeS** conjugates a thiol-sugar to the target via a disulfide bond




- Selenium-mediated chemistry
- Simple, fast, high-yield (~100%) reaction
- Compatible with physiological buffers
- Orientation mimics natural linkage
- Applicable to other acceptors with thiols, not just proteins

**GlycoExtend** enzymatically adds to the conjugated sugar with additional residues if required

# Current Pipeline

GlycoForm Programme	Therapeutic Indication	Discovery and Proof of Principle	Lead Optimisation	Pre-clinical	Clinical
GLY510	Anaemia				
GLYmAb	Cancer mAb				
scFv / peptides	Multiple				

## Legend

-  In-house
-  Collaboration with Cambridge Antibody Technology
-  In-house and collaborations

# Erythropoietin Background

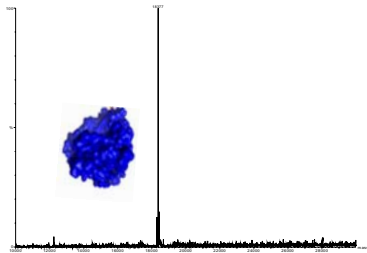
- Erythropoietin (EPO) is a glycoprotein hormone produced by the kidney that stimulates red blood cell production
- Recombinant EPO is used therapeutically to treat anaemia in renal disease, cancer and other conditions
- Manufactured by mammalian cell culture in CHO cells as a mixture of glycoforms



Stübiger et al *Rapid Commun. Mass Spectrum.* **2005**, 19, 728–742

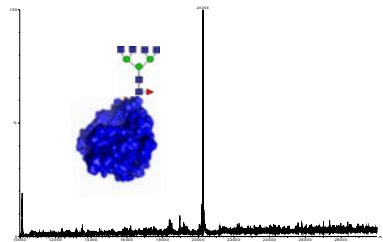
Multiple glycoforms of EPO- $\alpha$  as shown by MS

# GLY510 for Anaemia: Stepwise Synthesis



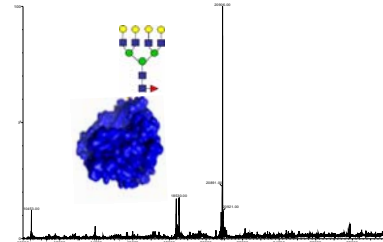
Found 18377  
Theor. 18381

A single cysteine glycosylation site mutant GLY510 is made in *E. coli*



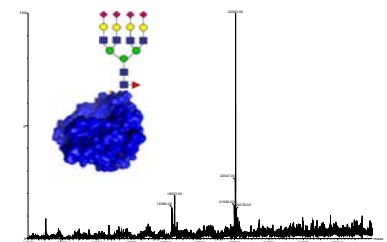
Found 20258  
Theor. 20264

Thiodecasaccharide is conjugated to protein using GlycoSeS



Found 20906  
Theor. 20912

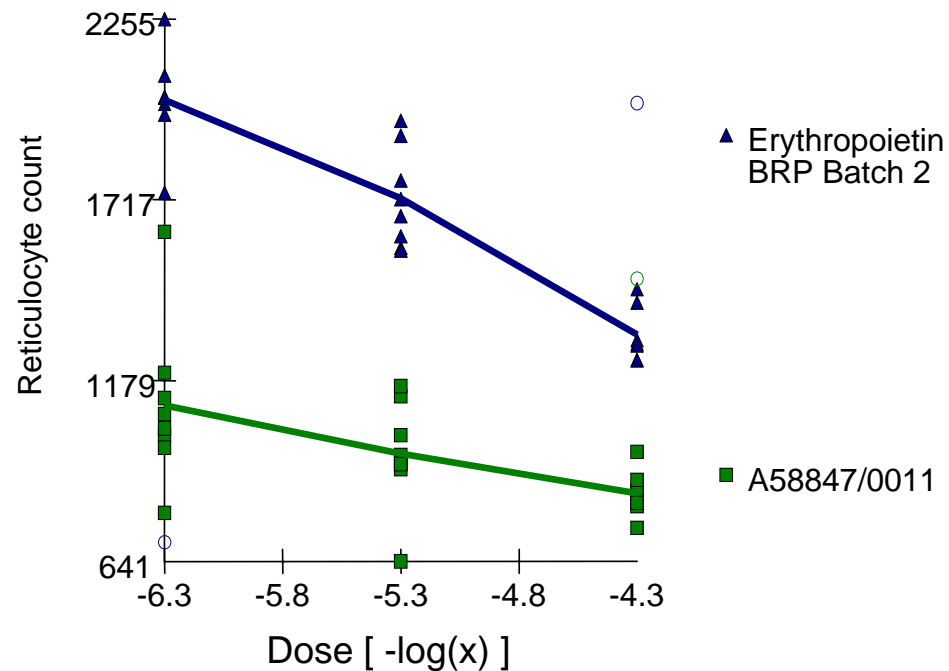
Carbohydrate is extended enzymatically with 4 galactoses



Found 22063  
Theor. 22076

Further enzymatic extension with 4 sialic acids yields final product of striking homogeneity



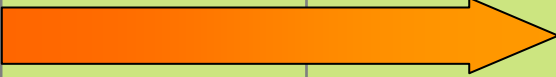


# Proof of Principle: Animal Efficacy







GLY510 Stimulates Erythropoiesis in normocythaemic mice assay

Assay is a standard EPO batch release assay which measures activity through reticulocyte count

# Pipeline Development at 2010

GlycoForm Programme	Therapeutic Indication	Discovery and Proof of Principle	Lead Optimisation	Pre-clinical	Clinical
GLY510	Anaemia				
GLYmAb	Cancer mAb				
Fragments / Peptides	To be determined				
Pharma collaboration 1	To be determined				
Pharma collaboration 2	To be determined				

## Legend

-  In-house
-  Collaboration with Cambridge Antibody Technology
-  In-house and collaborative
-  Large Pharma Partnering

## Cancer antibodies

- The relationship of glycosylation pattern to biological activity (ADCC) is well established
- Early stage collaboration ongoing with CAT (AstraZeneca)

## Peptides

- GlycoForm technology could be enabling for this problematic class (improve affinity, increase half-life, target specific tissues, increase stability)
- Collaboration established on scFv; in discussion on smaller peptides

## New Projects

- Collaborations to be established; discussions are ongoing

## **Significant valuations have been made for companies with glycoengineering platforms**

- GlycArt purchased by Roche for \$200 million in 2005
- GlycoFi purchased by Merck for \$400 million in 2006

## **Acquisitions and licensing deals allow exclusive access to technology**

## **GlycoForm's business model is well positioned to fulfil the needs of drug companies**

- To access new technologies to develop novel biotech drugs
- To develop next-generation products for franchise management

# Positioned for Success



Strong market with unmet clinical needs

Proof of principle of the platform has been demonstrated

Collaborator programme established with Cambridge Antibody Technology

An experienced team

£5 million sought to advance a powerful business model with risk-reduced strategy



# GlycoForm

Novel Synthetic  
Glycoproteins

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