



# Ancora Pharmaceuticals Inc.

The 3<sup>rd</sup> Glycan Forum in Berlin

A. Stewart Campbell

## Synthetic Carbohydrate Antigens:

Enabling a New Paradigm in Vaccine  
Development

**Berlin, Germany**  
**February 22-23, 2007**



# Ancora Pharmaceuticals Overview

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- Privately held, Medford-based company started in 2003

- Carbohydrate synthesis technology developed at MIT; continued at ETH-Zurich



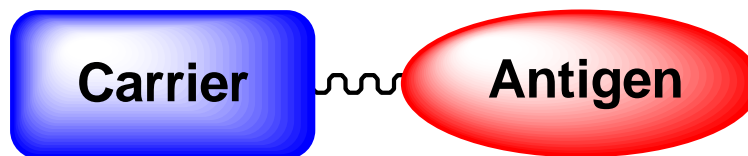
- Carbohydrate based custom service and product discovery focus

# Carbohydrate-Based Applications

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## Vaccines

(polysaccharides, glycoconjugates)



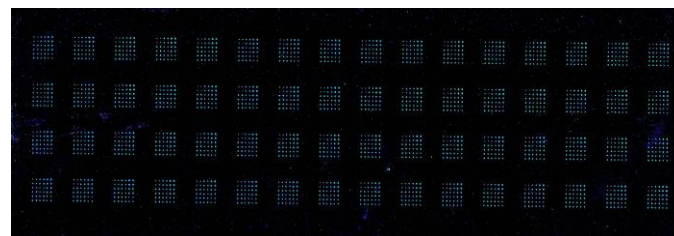
## Therapeutics

(heparins, endotoxin antagonists)

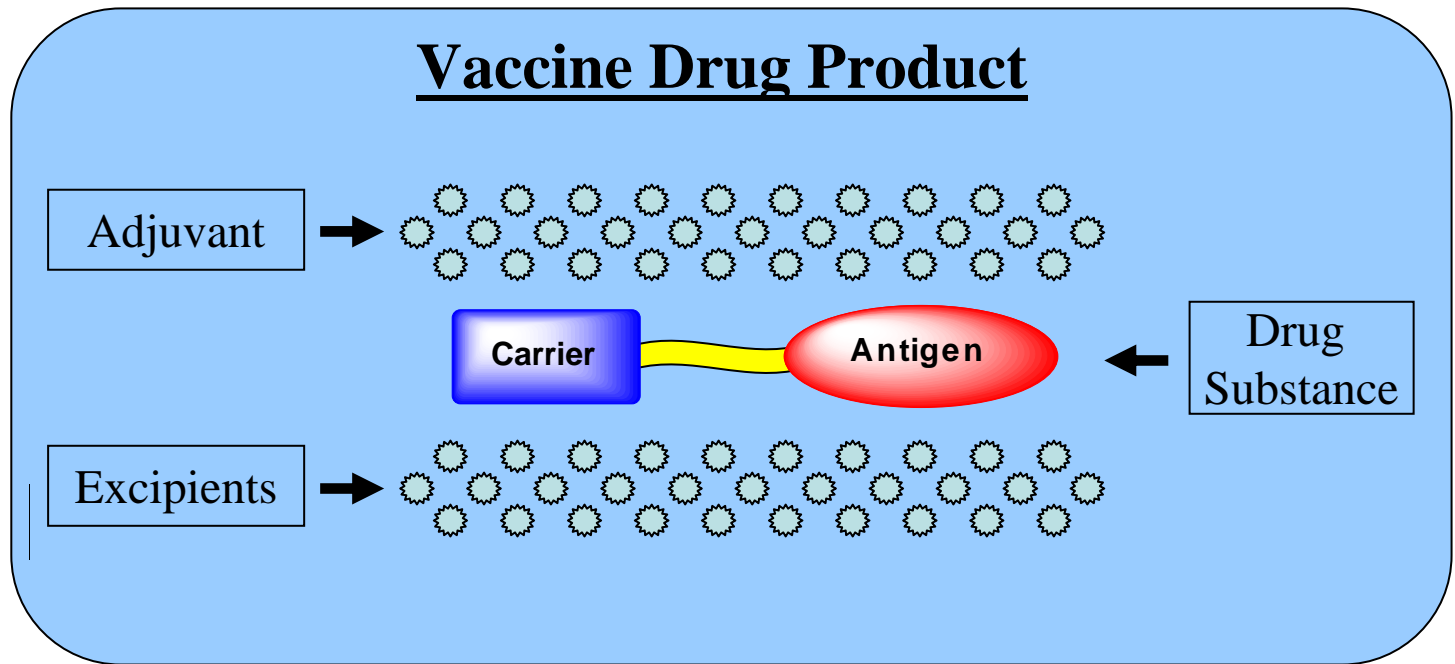


## Glycomics

(biomarkers, diagnostics)



# Conjugated Carbohydrate Vaccines



T-Cell independent response  
Poor memory

T-Cell dependent response  
Immunological memory

# Evolution of Carbohydrate-Based Vaccines

1970's-1980's

**Polysaccharides**

Menomune (Sanofi, 1978)

1980's-today

**Conjugated Poly/Oligosaccharides**

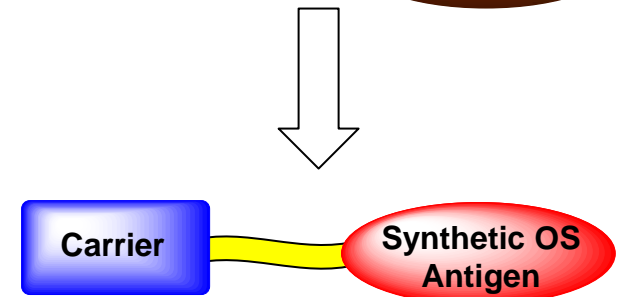
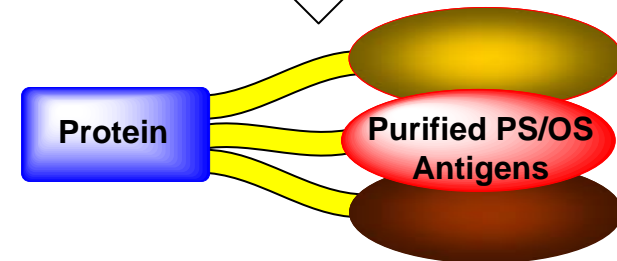
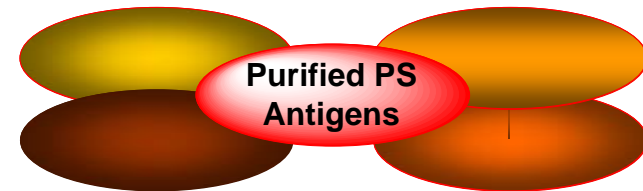
Menactra (Sanofi, 2005)  
Menjugate (Novartis)  
Meningitec (Wyeth)

2003 →

**Conjugated Synthetic Oligosaccharides**

???

Vaccines Drug Substance

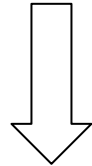


# Evolution of Carbohydrate-Based Vaccines

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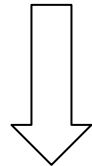
*1970's-1980's*

**Polysaccharides**



*1980's-today*

**Conjugated Poly/Oligosaccharides**

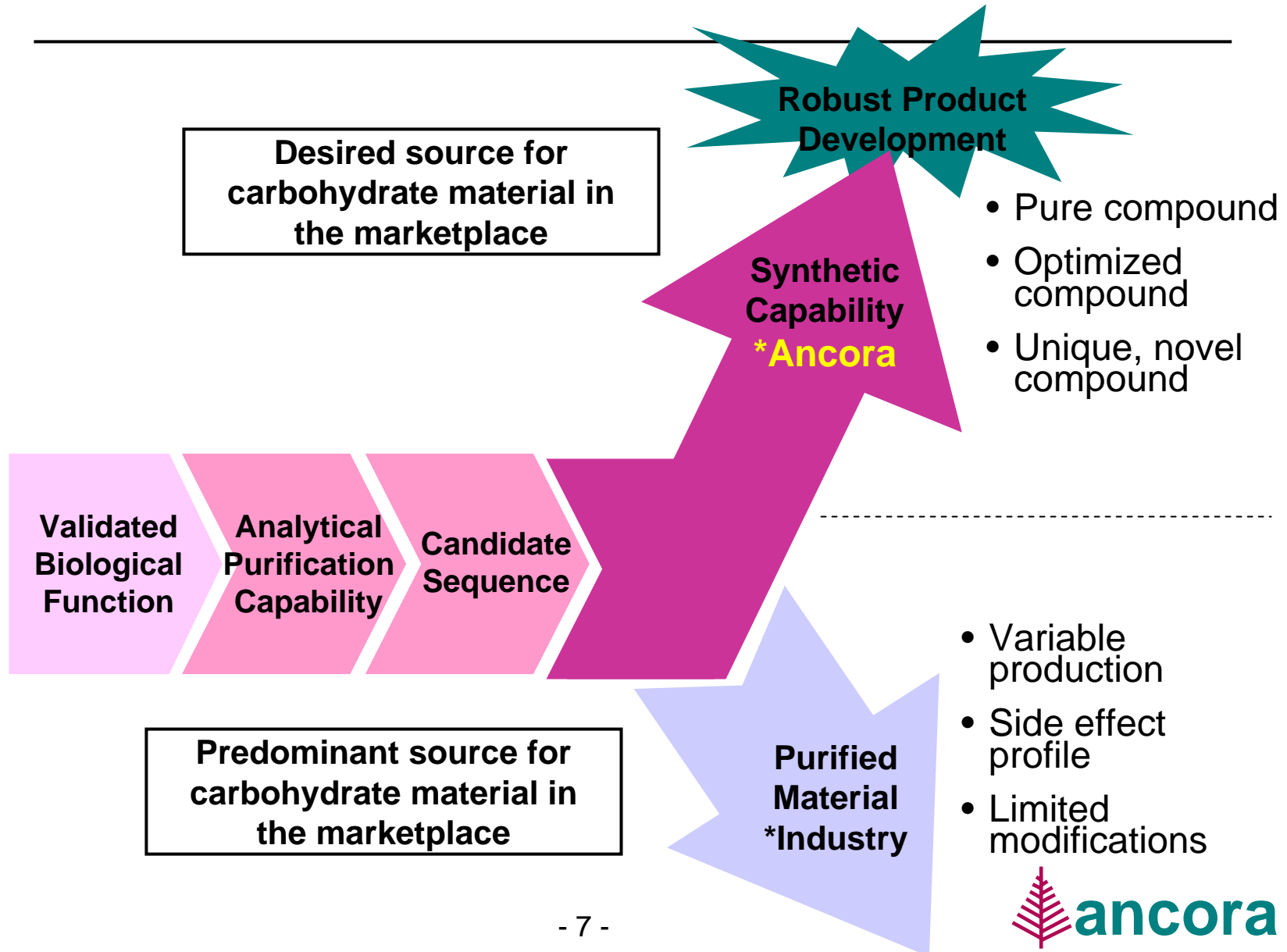


*2003 →*

**Conjugated Synthetic Oligosaccharides**



# Why Synthetic Carbohydrate Antigens?



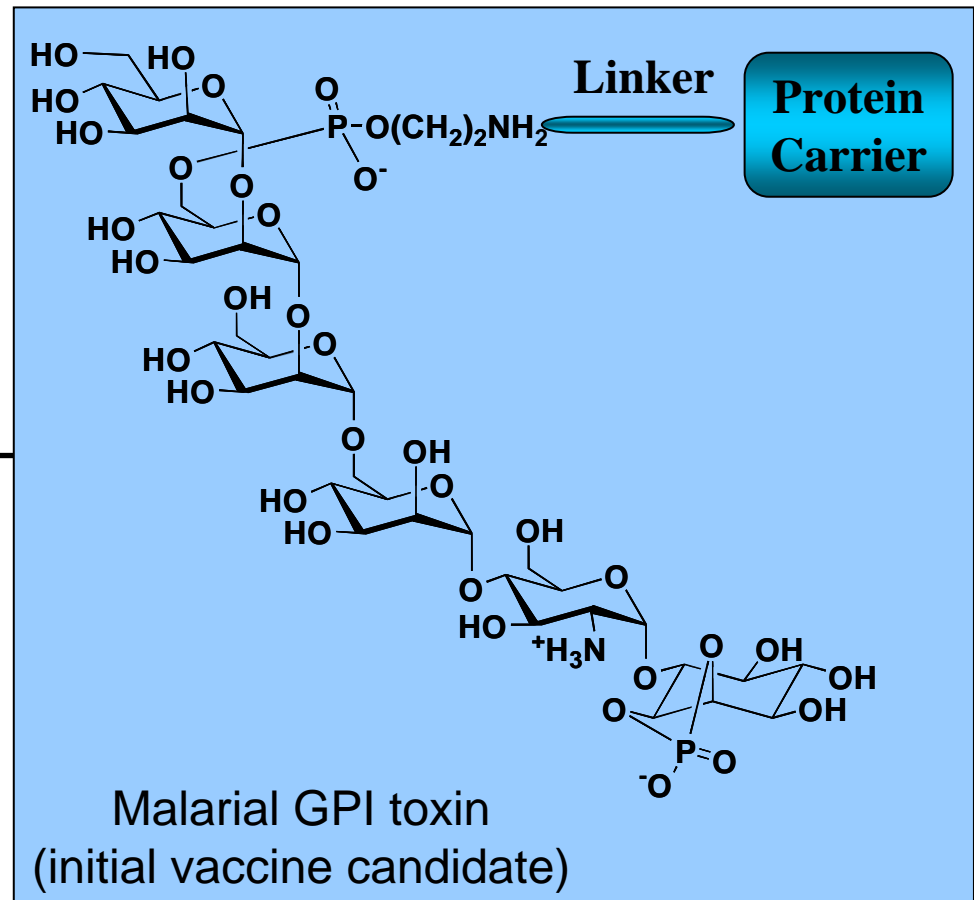
# Synthetic Carbohydrate Antigen Development Challenges

- Candidate optimization
- Pre-clinical scale
- Regulatory Process

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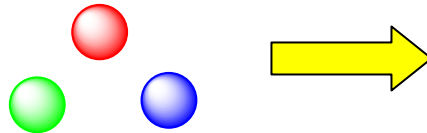
- Commercial scale
- Process reproducibility
- Process cost

Example: GPI Malaria Vaccine Antigen

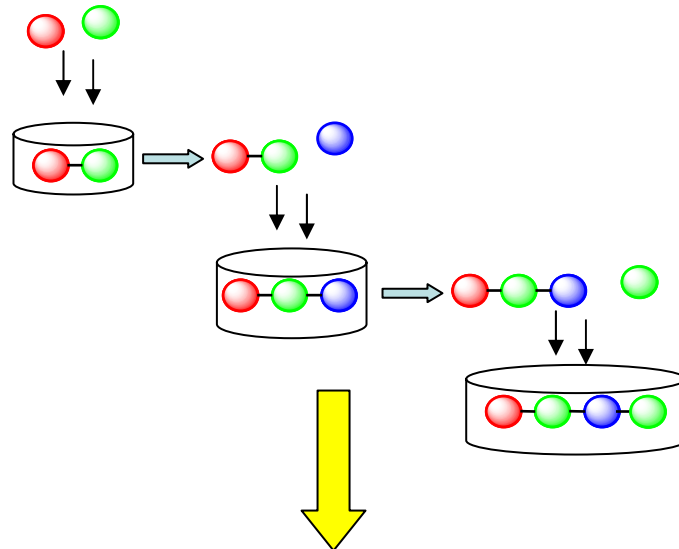


# Ancora Enabling Technology

**Building Blocks  
(Input)**

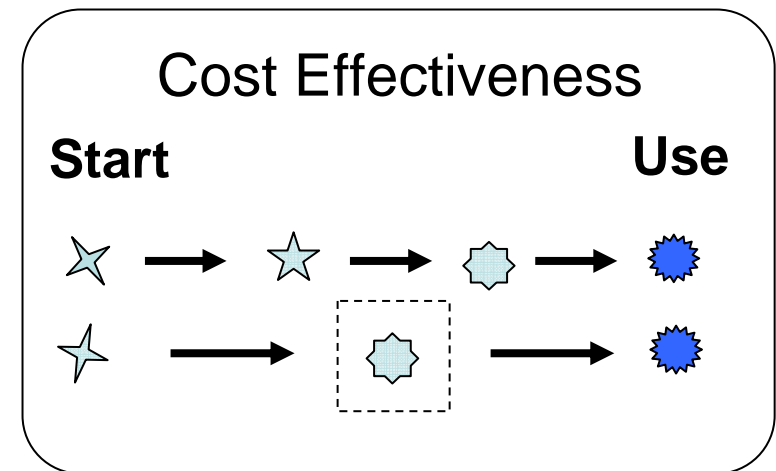
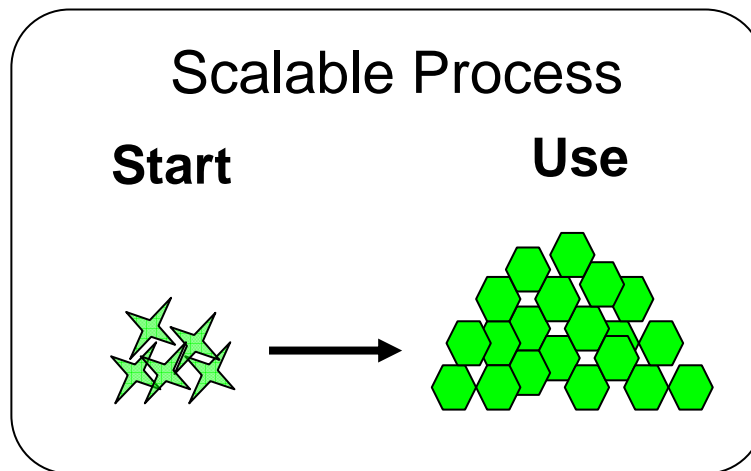
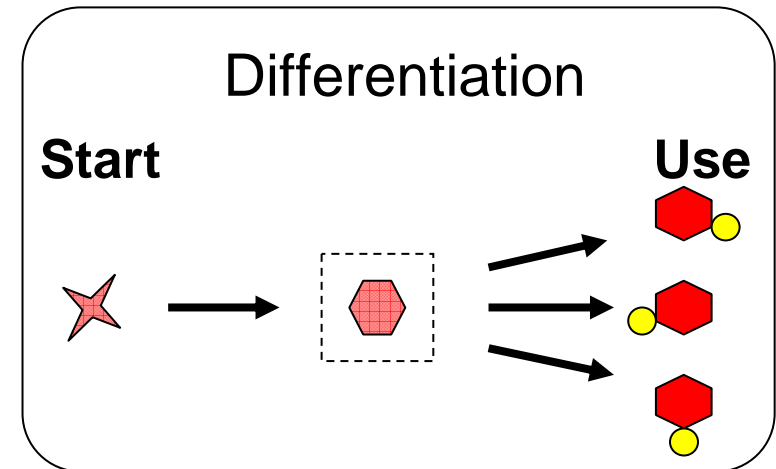
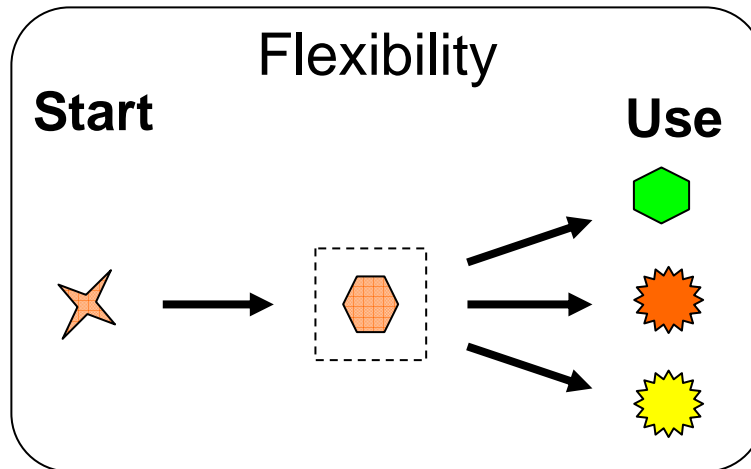


**Assembly Technology  
(Process)**



**Complex Carbohydrates  
(Output)**

# Parameters for Building Block Solutions



# Building Block Example: Mannose Unit of Malaria Vaccine Antigen

## Initial process scheme

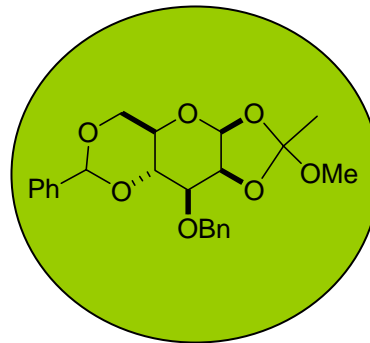
**5 synthetic  
steps**

**3 Column  
Purifications**

**Up to 50 grams**

**35% Yield**

## Orthoester



## Optimized process scheme

**5 synthetic  
steps**

**0 Column  
Purifications**

**Kilogram scale**

**60+% Yield**

# Building Block Example: Inositol Unit of Malaria Vaccine Antigen

## Initial process scheme

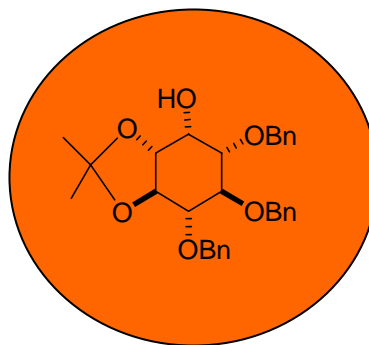
**8 synthetic steps**

**6 Column Purifications**

**milligrams**

**Limited resolution**

## Inositol



## Current process scheme

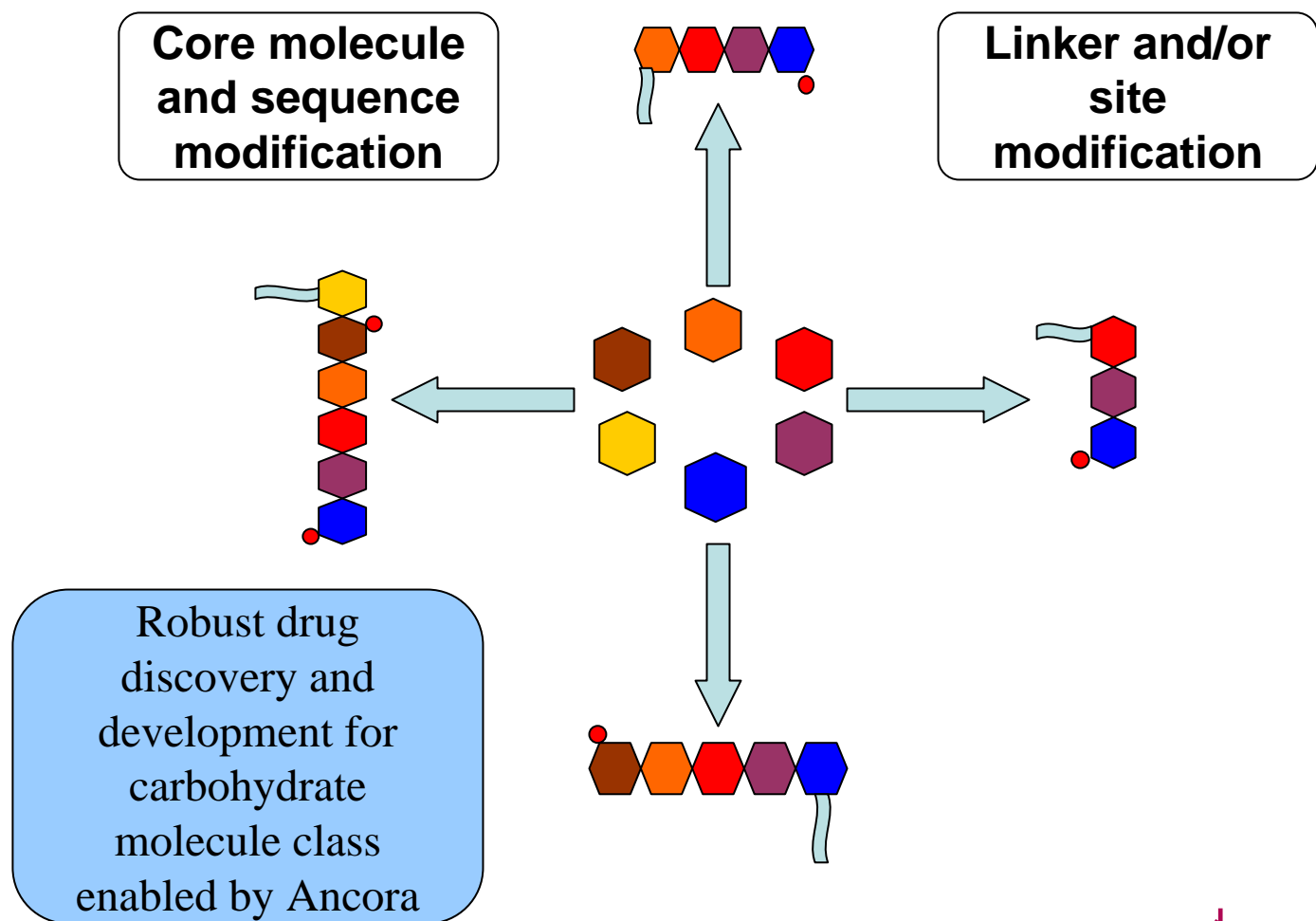
**6 synthetic steps**

**1 Column Purification**

**Kilogram scale**

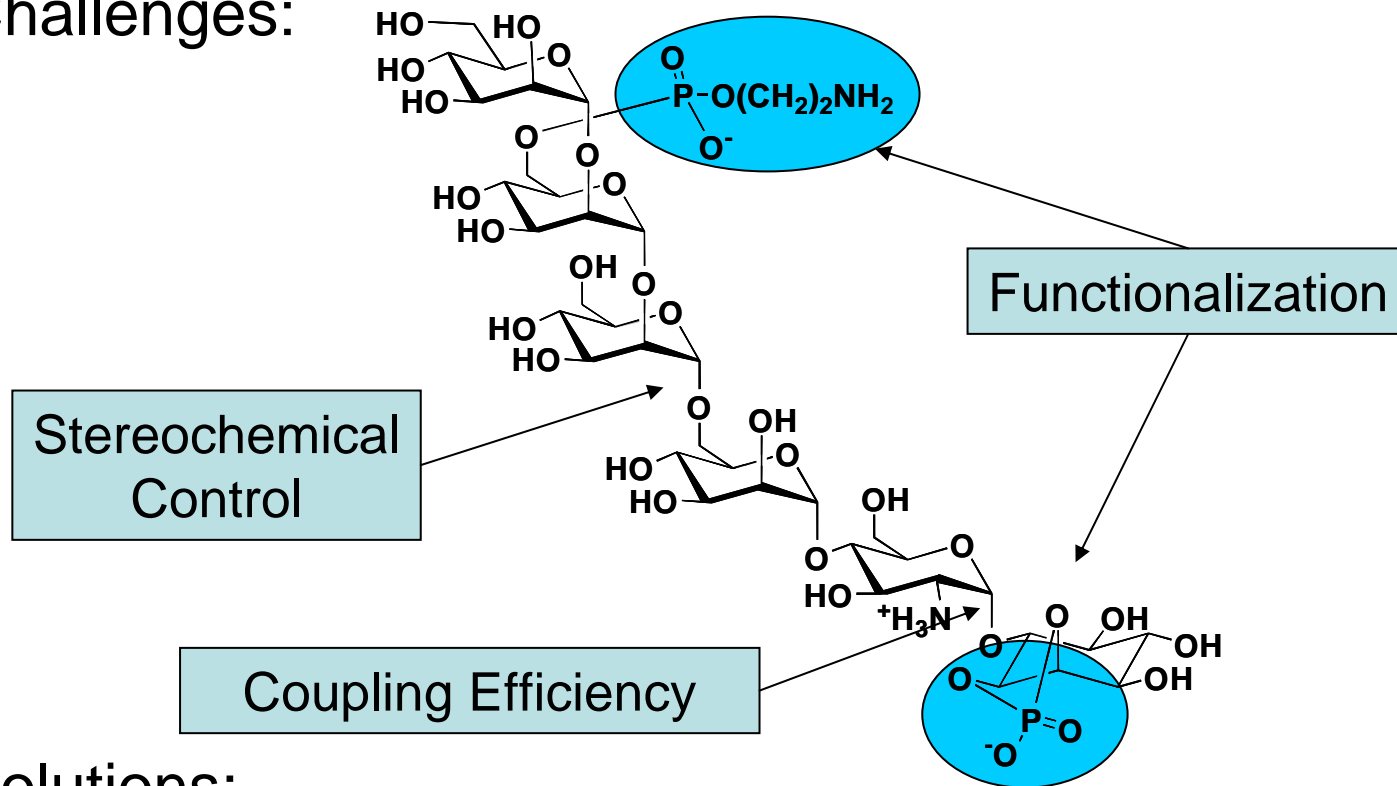
**Facile resolution**

# Building Block Technology Enables Carbohydrate Molecule Optimization



# Carbohydrate Assembly Considerations

Challenges:



Solutions:

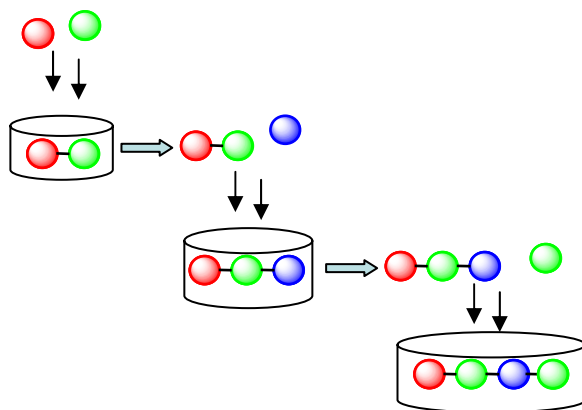
Reproducible and scalable processes

Flexible introduction of functionality

Robust final purification

# Ancora Assembly Technologies

## Solution Phase

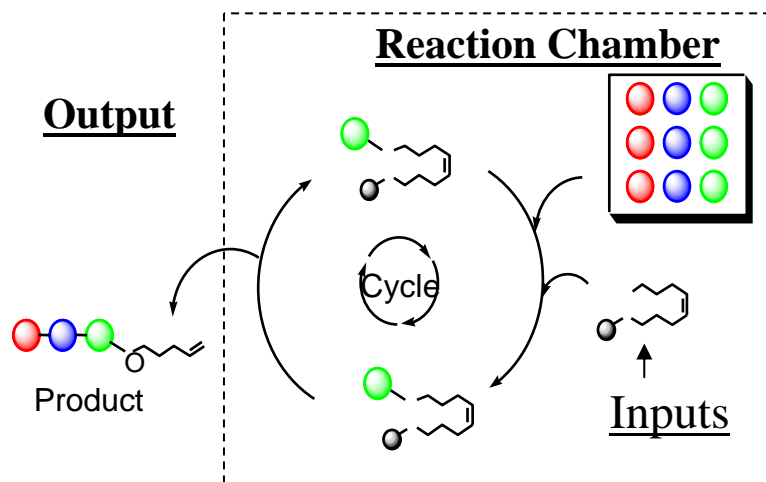


Unlimited chemistry

Scalability

Adaptable to industry

## Solid Phase



Amenable to automation

End stage purification

Rapid process

# Automated Synthesizer Development

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## Major system criteria

Fine volume  
control

Fine temp.  
control

Anhydrous  
environment

Readily  
scalable

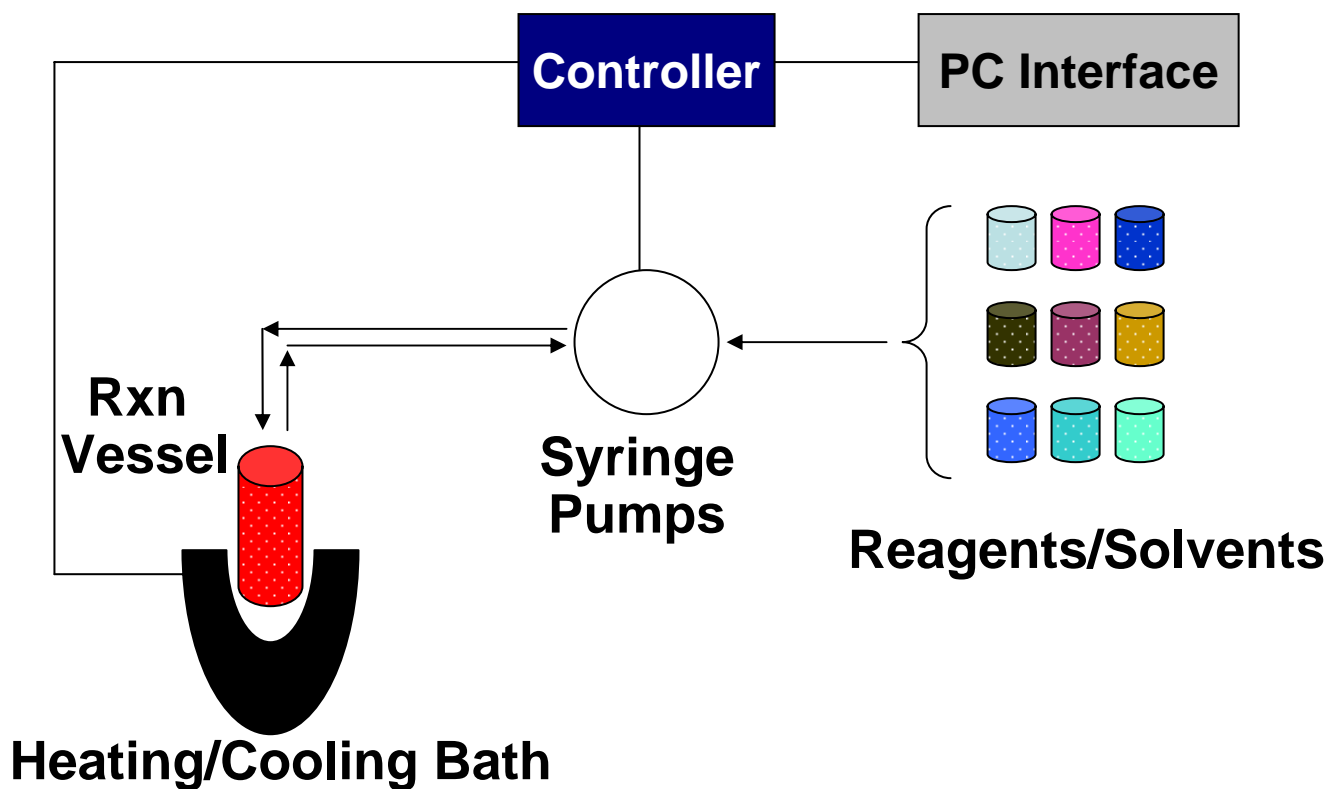
Full  
automation

Cost effective

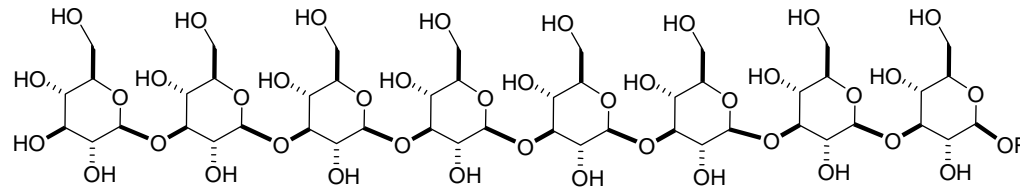
Customization of existing commercial  
systems not practical

# Automated Synthesizer Schematic

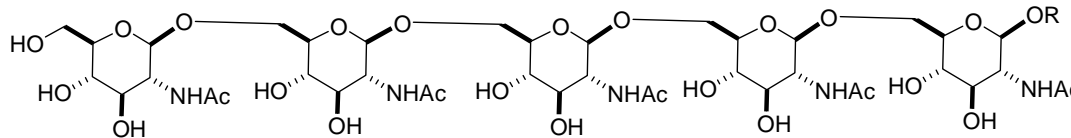
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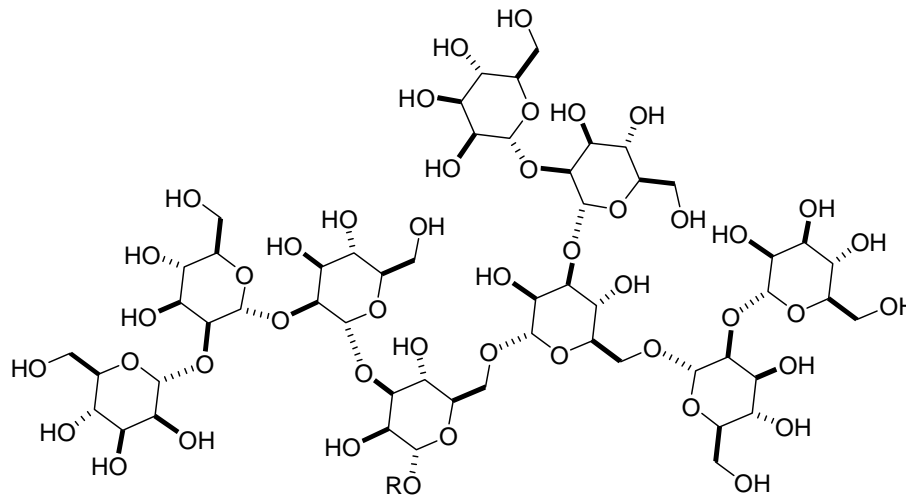
# Examples of Other Classes of Synthetic Antigens



$\beta$ -Glucans:  
*Candida*

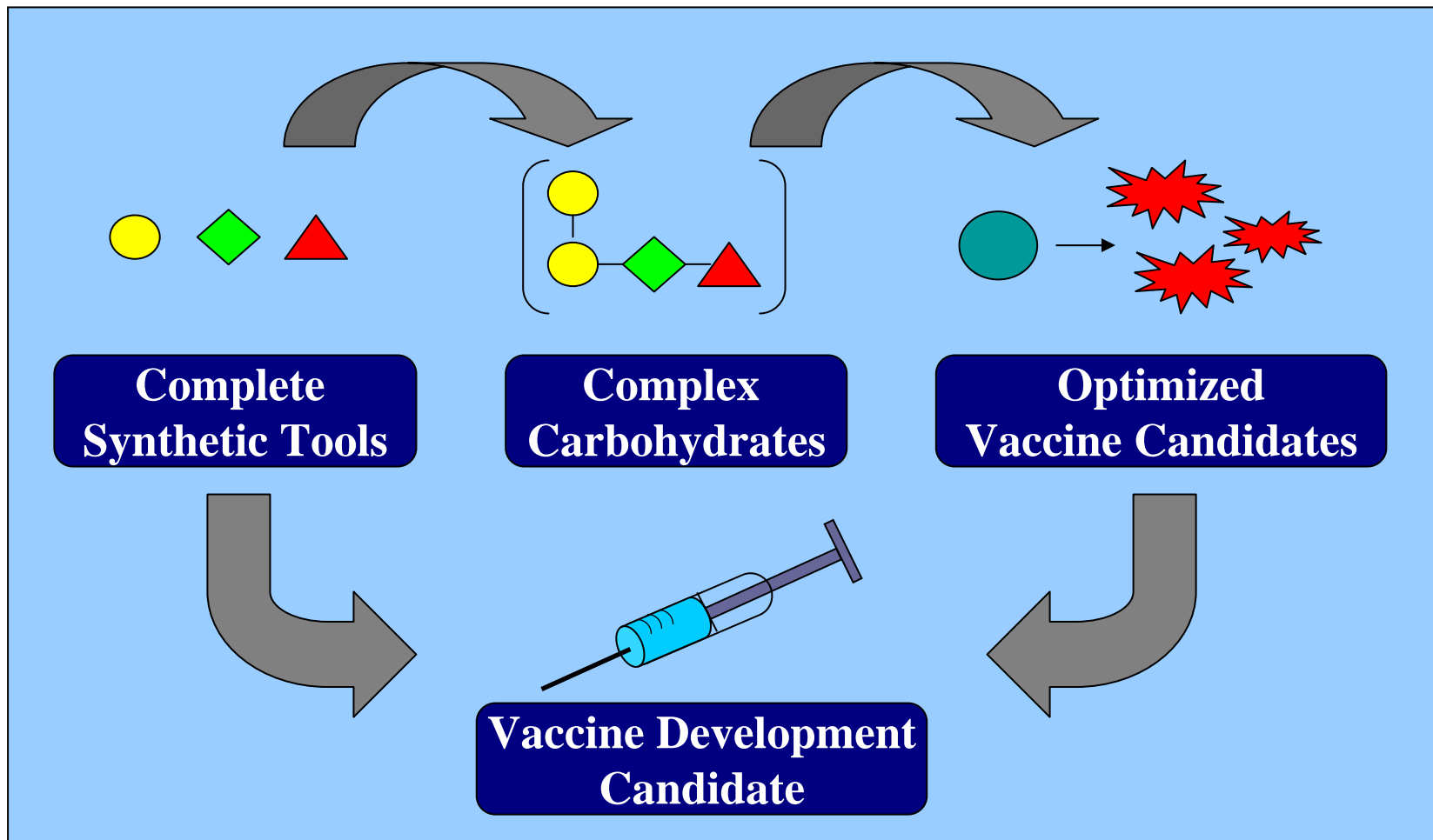


Poly-glucosamines:  
*S. aureus*



High Mannose:  
HIV, Leishmania

# Summary: Coherent Strategy Toward Synthetic Carbohydrate Vaccines



# Acknowledgements

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## Ancora

Dr. John Pena  
Dr. William Christ  
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Yuhong Guo  
Matthew Jones

## Advisors

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Prof. Louis Schofield, WEHI