Genomatica

- Sustainable chemicals
- Better economics
- Smaller footprint

Pacific Rim Summit on Industrial Biotechnology & Bioenergy
October 10-12, 2012

Nelson Barton, VP R&D

A Process for the Production of Bio-based 1,4-Butanediol (BDO)
## Genomatica at a Glance

### The Company
- Private company
- San Diego (USA)
- 105 people

### Bio-Based Chemicals
- Basic/intermediate chemicals
- Technology provider

### Top Financial Investors
- Raised $125 MM to date

### Partnering with Industry
- Global commercialization
  - feedstocks, scale-up, applications
Low-Cost Renewable Feedstock

- sugars
- biomass
- syngas

High Performance Organisms

- High titer, Tolerance
- High yield
- High productivity

Basic & Intermediate Chemicals

- Existing products sold globally

Genomatica: Focused on Bio-based Chemicals

- Exact same chemicals
- Better economics
- Equivalent performance
- Reduced energy
- Lower carbon footprint
- Feedstock diversification

Direct production of chemicals likely to afford lowest cost process
Bio-based 1,4-Butanediol

Crude Oil & Nat. Gas → Acetylene → Propylene → Butane, Butadiene

Sugars → Direct Production

BDO (1,4-Butanediol)

3 B lb/yr existing market

spandex
polyurethans
PBT

genomatica sustainable chemicals
Advantages of Identical Drop-in Bio-BDO

- Downstream infrastructure in place
- Can blend with existing BDO
- Faster adoption
- Meet customer needs for renewable products

Fermentation → BDO (1,4-Butanediol) → Existing Infrastructure → Direct Replacement

Applications

PBT Pellets from Bio-BDO

genomatica sustainable chemicals
Genomatica’s BDO Process in Engineered *E. coli*

Sugars

BDO-producing *E. coli*

1,4-Butanediol (Bio-BDO)

100% bio-based content

Strain, fermentation, process engineering → deliver BEP

Tate & Lyle facility
Journey to a BDO Production Strain

Pathway Identification and Engineering

Strain Design and Metabolic Engineering

Commercial Strain for BDO Production

Fermentation Metrics → Higher TRY = Lower COGS

- **Titer (g/L)** - Impacts equipment sizing and energy needs
- **Rate (g/L/h)** - Impacts # of fermentors, plant capacity
- **Yield (g/g)** - feedstock cost, by-product cost in DSP
Commercial Strain Engineering Challenges

- Major Challenge – High Titer, Rate, Yield – “It is all about the Bug”
- Define commercial TRY targets needed to achieve desired economics

**Minimal defined media**
Lower cost, ensure cellular requirements satisfied
Minimize salts to DSP

**Fast growth**
Minimal lag

**Increase rate**
Improved enzymes
Lower by-products
Sugar uptake rate
Aeration, co-factor balance

**Delay production slowdown**
Nutrient limitation
Osmolarity
Tolerance, Stress
Enzyme inhibition

**Genetically stable host**
Fully integrated – no plasmids
Pathway expression – Constitutive or “no cost” induction

**Target Titer**

**Titer (g/L)**

**Time**
Genomatica’s Systems-Based Strain Engineering

- Select Parent strain
- Synthesize Biology Tools
- HT Cloning
- Pathway & Strain Design
- Analyze & Interpret
- Omics data
- Systems analysis
- Genomics
- Metabolomics
- Proteomics
- Transcriptomics
- 13C-Fluxomics

- Biological Knowledge
- Iterative Strain Engineering
- LIMS

- Data
- Engineered strains
- Fermentation development/scale-up
- HT Screening In vivo assays
- By-product deletions
- Regulatory network engineering
- Transporter engineering
- Pathway engineering
- Removal of negative regulation

- Enzyme Evolution
- Whole Cell Mutagenesis

- Computational Technologies

- Product Feedstock Organism & Tools

- Product Feedstock Organism & Tools
BDO Strain Engineering Progress

- April, 2012: 108 g/L
- Feb, 2012: 1.2 M
- Oct, 2011: 2.5 g/L-h
- May, 2011: 1.2 M
- Mar, 2011: 108 g/L
- Jan, 2011: 2.5 g/L-h

2011: 108 g/L
2012: 1.2 M
Increasing Rate and Lowering By-products

Key Advances
- Eliminate backflux
- Improved enzymes
- Redox supply
- ATP supply
- Regulation
- Balanced expression
- Fermentation PD

More metabolic steps in a pathway increases avenues for by-products
Lowering By-Products: Excess CO₂

C₆H₁₂O₆ + 0.5 O₂ → C₄H₁₀O₂ + 2 CO₂ + H₂O

- Excess CO₂ from complete TCA
- Delete sucCD gene – lose 1 ATP
- Eliminated “futile” energy drains
Lowering Excess CO$_2$ via $\Delta$sucCD Deletion

$\Delta$sucCD Strain: higher BDO, much lower CO$_2$
BDO Scale-up and Commercialization

Joint Development Partnership with Tate & Lyle

TATE & LYLE

- $4.3B per year
- Operates four corn wet mills
- JV with DuPont: PDO, 100-140M lb/yr

Genomtica taking proven path:
✓ Same base organism
✓ Same scale-up factor
✓ Similar chemical
✓ Similar cost model

13,000 L fermentor in Decatur demo plant
Complete Process Technology for Bio-BDO

Successful customer conversions
• No reformulation
• Can blend with existing BDO

High Purity Bio-BDO
- Completely Compatible
- >99.9% pure
- No color (< 10 APHA)
- Water < 100 ppm
- GBL = <1 ppm
- Sulfur < 1 ppm
Shipping tons at a time…
Bio-BDO® Becoming a Commercial Reality

2008
first production of 1,4-BDO from carbohydrates

2013
commercial scale production (40M lbs/yr)

High quality Bio-BDO converted into all downstream derivatives by partners

PBT from Bio-BDO

Genomatica sustainable chemicals
Novamont: BDO in Europe

- Joint venture for commercial-scale production of BDO
- Novamont financing 100% of construction costs (~$50M)
- Begin production 2013
- 40 million pounds per year
- Committed to purchase 100% of production for captive use
- Option for second plant
Biomass-to-Chemicals

Biomass sugars offer:
- Lower price volatility
- Lower cost potential
- No food vs chemicals

Biomass-to-BDO
- $5 M DOE Grant

Currently producing BDO in *E. coli* from PROESA biomass sugars at ~85% of performance vs dextrose
Development of a Robust BDO Production Strain

- Systems-based approach
- Over 35 genetic manipulations
- BDO from dextrose, sucrose, biomass
- Achieved commercial TRY targets
- Process scale-up to 13,000 L (1 ton/wk)
Genomatica BDO Team - Past and Present

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Christophe Schilling, CEO  Bill Baum, CBO  Mark Burk, CTO  Jeff Lievense, EVP, Process Development
Questions?

Thank you