Turning the promise of synthetic biology into commercial reality for health and energy

European Comission Synthetic Biology Workshop, 18 March 2010

Joel R. Cherry
SVP, Research Programs and Operations
Amyris Biotechnologies Inc.  
Leading the “next generation” of renewable products

► Started in 2004 by four postdocs from UC Berkeley Professor Jay Keasling’s lab

► Initially funded in 2005 by a grant from the Gates Foundation to develop a lower cost, consistent supply of artemisinin

► Venture funded by leading investors; over $160MM in grants and equity financing

► Pioneering yeast technology enabling production of more than 50,000 hydrocarbon molecules

► Product portfolio - anti-malarial drug, diesel, jet fuel and a wide-range of chemicals

► Issued US patents covering diesel, jet, and lubricant products

► Marketing and distribution channels to deliver products in the United States and other global markets
Overview
Technology Enables Broad Product Opportunities

Traditional oil source

![Oil](image1)

+ ![Refinery](image2)

= **Petroleum products**

- **diesel**
  - 2020 estimate 450 billion gallons

- **jet fuel**
  - 2020 estimate 124 billion gallons

- **specialty chemicals**: synthetic rubbers, lubricants, etc.

Amyris renewable pathway

- **Sugar cane**
- **Amyris genetically engineered yeast**
- **Cane mill**

= **> 50,000 isoprenoid compounds**

- **malaria drug**
  - *non-profit: treat over 200 million people annually*

• Markets growing faster than GDP
• Chemicals price point not directly correlated to price of crude oil
• Structurally advantaged, low-cost producer
A platform technology for production of multiple products

Sucrose → Acetyl-CoA → Mevalonate pathway → Mevalonate → IPP → FPP → Terpene Synthase → Jet/Gasoline Precursors

Acetyl-CoA → Mevalonate pathway → Mevalonate → IPP → FPP → Terpene Synthase → Jet/Gasoline Precursors

Artemisinic Acid

Diesel and chemical precursor

Jet/Gasoline Precursors

Anti-Malarial Drug First Sale 2011

Sucrose

Mevalonate

IPP

FPP

Terpene Synthase

Isoprene

Mevalonate pathway

Acetyl-CoA

H₂C

SCoA

H₂O

H₂O
April, 2008 - Announced partnership with sanofi-aventis for microbial artemisinin

- Nonprofit project
- Lives saved due to scalable supply of inexpensive drug
- $20+MM to develop a platform for isoprenoid production
Amyris process for microbe development
Engineering cycle to increase performance

Programmed chemical conversion

Sugar → Yeast → Chemical Products

Knowledge management

Ideation, Construction, Screening, Analytics

Farnesene

ERG10, ERG12, HMGR, ERG16, ERG20, IDI1, ERG13, ERG10, tHMGR
The heart of synthetic biology is standardization

• **Tool Standardization**
  Consistent, simple and reliable enzyme
  and/or chemical treatments for the genetic manipulation of organisms

• **Parts Standardization**
  Genetic elements that can be easily interchanged using the same
  or similar tools

• **Process Standardization**
  Consistent, simple and reliable methods for
  the insertion and deletion of genetic elements
Standardization & Automation of Strain Engineering
Rapid, reliable microbial engineering

**Traditional construction**

1. Labor intensive planning
2. Hand crafted construction
3. Relatively slow, expensive, error-prone
4. 4 week cycle, 40 strains per cycle with 4 FTEs

**Automated construction**

1. Computer assisted design
2. Robotics platform for unit operations
3. Fast, inexpensive, reliable
4. 6 week cycle, 5000 strains per cycle with 4 FTEs
Automated strain engineering is a reality at Amyris

Computer aided design (CAD) & RYSE

Automated rational strain engineering

HTP Screening

Production in Brazil

300 liter fermentation

2 liter fermentation
The first run of ASE
WHY? Automated strain engineering standardizes parts, reduces failure rates, decreases costs, increases strains tested.

- **Traditional strain engineering**
  - 250 strains/month
  - 10 strain/biologist/month
  - $2,400/strain
  - First attempt success rate: 70%

- **Automated strain engineering**
  - 5000 strains/month with 4 FTE’s
  - 1000 strains/biologist/month
  - $60/strain
  - First attempt success rate: 90%
The payoff: Better strains faster
Fermentation derived hydrocarbons = lower processing costs
Production at scale: lab to pilot to commercial

1st barrels of Amyris Renewable Diesel from Pilot Plant, Q1 2009

Demo Plant Fermenter, Campinas Brazil Q2 2009

Production at 60,000 L scale, Q2 2009
Products – Renewable Fuels and Chemicals
Diesel fuel registered with the EPA at a 20% blend

Cloud Point
degrees Celsius

-9 to -30  # 2-D
-75 -50 -25 0

< - 50  Amyris

+1  SME

Cetane Number

# 2-D

0  20  40  60

40-55

# 2-D

Amyris

47

SME

Amyris

58.1

Energy Density
1000 BTU/gal

# 2-D

0  50  100  150

115-142

SME

118

Amyris

121

Additional benefits of Amyris renewable diesel compared to #2-Diesel
• 90%+ lower greenhouse gas emissions
• No sulfur
• produces lower NOx and particulate emissions

Note: Amyris diesel will be used in blends with conventional fuels; values shown for Amyris diesel is for our biomass derived blending component; SME = Soy Methyl Esters
Participation in the value chain

Amyris will participate in various aspects along the biofuels value chain

- **Feedstock**
- **Technology**
- **Manufacturing**
- **Product Transportation & Logistics**
- **Terminal & blend racks**
- **Retail Customers**
- **Commercial Customers**

**Amyris GreenLane™**

**Partner with large scale manufacturer with access to low cost feedstocks**

**Build production platform from distressed assets**

**Take product from plant gate to wholesaler**
- Logistics contracts to facilitate high volume distribution

**Sell to fastest growing retail segment**
- Access to end customers (commercial accounts)
Critical path to 2011 – commercial plant in Brazil

Ethanol Distillation → Juice Clarification Pre-Evaporation → Ethanol Fermentation → Cane Mill

Suggested site (recent)
# Plan to commercial production – timeline

<table>
<thead>
<tr>
<th>Year</th>
<th>Event</th>
</tr>
</thead>
<tbody>
<tr>
<td>2009</td>
<td>R&amp;D center inaugurated in 2008 in Campinas&lt;br&gt;Q2: Pilot plant operational; Demo Facility opened&lt;br&gt;Q4: Acquire EtOH Mills&lt;br&gt;  - Ongoing operations provide immediate revenue and cash flow</td>
</tr>
<tr>
<td>2010</td>
<td>Begin mill conversion to produce Amyris renewable products&lt;br&gt;  - Engineering of commercial plant has been finalized and EPCM has been engaged</td>
</tr>
<tr>
<td>2011</td>
<td>First large scale production of Amyris renewable products&lt;br&gt;Continue mill conversion and expansion</td>
</tr>
<tr>
<td>2012</td>
<td>First commercial production by third party mills under “capital light” strategy</td>
</tr>
</tbody>
</table>

---

*Do Not Distribute Without Prior Authorization*
Take-home messages

• Standardization of parts, tools and processes has facilitated automated strain engineering
• ASE is game changing for the development of renewables
• Amyris is on track for 2011 commercial production of diesel and chemical products
Thanks for listening
Disclaimer

This paper was produced for a meeting organized by Health & Consumers DG and represents the views of its author on the subject. These views have not been adopted or in any way approved by the Commission and should not be relied upon as a statement of the Commission's or Health & Consumers DG's views. The European Commission does not guarantee the accuracy of the data included in this paper, nor does it accept responsibility for any use made thereof.