

The logo for LYGOS, featuring the letters L, Y, G, and S in a bold, black, sans-serif font. The letter O is replaced by a green rounded square containing a white diagonal line from the top-left to the bottom-right.

**LYGOS**

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**Engineering yeast to convert  
sugar into high-value chemicals**

Jeffrey Dietrich, CTO and Co-Founder  
BIOENERGY 2016  
07/13/2016

# Introduction to Lygos

## Producing Malonic Acid Today

### Scaling Integrated Process

- **Founded 2010**
- **15 Employees**
- **Berkeley, CA**
- **2013:** Innovative Biosynthetic Pathways to Advanced Biofuels
- **2015:** Small Business Voucher
- **2016:** Bioenergy Technologies Incubator 2

**Eric Steen**  
CEO, PhD UCB  
Bioengineering

UCSF

Berkeley  
UNIVERSITY OF CALIFORNIA

jbei  
Joint BioEnergy Institute



**Jeffrey Dietrich**  
CTO, PhD UCB Bioengineering

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**Jay Keasling**  
Investor, Founder;  
Science Advisor

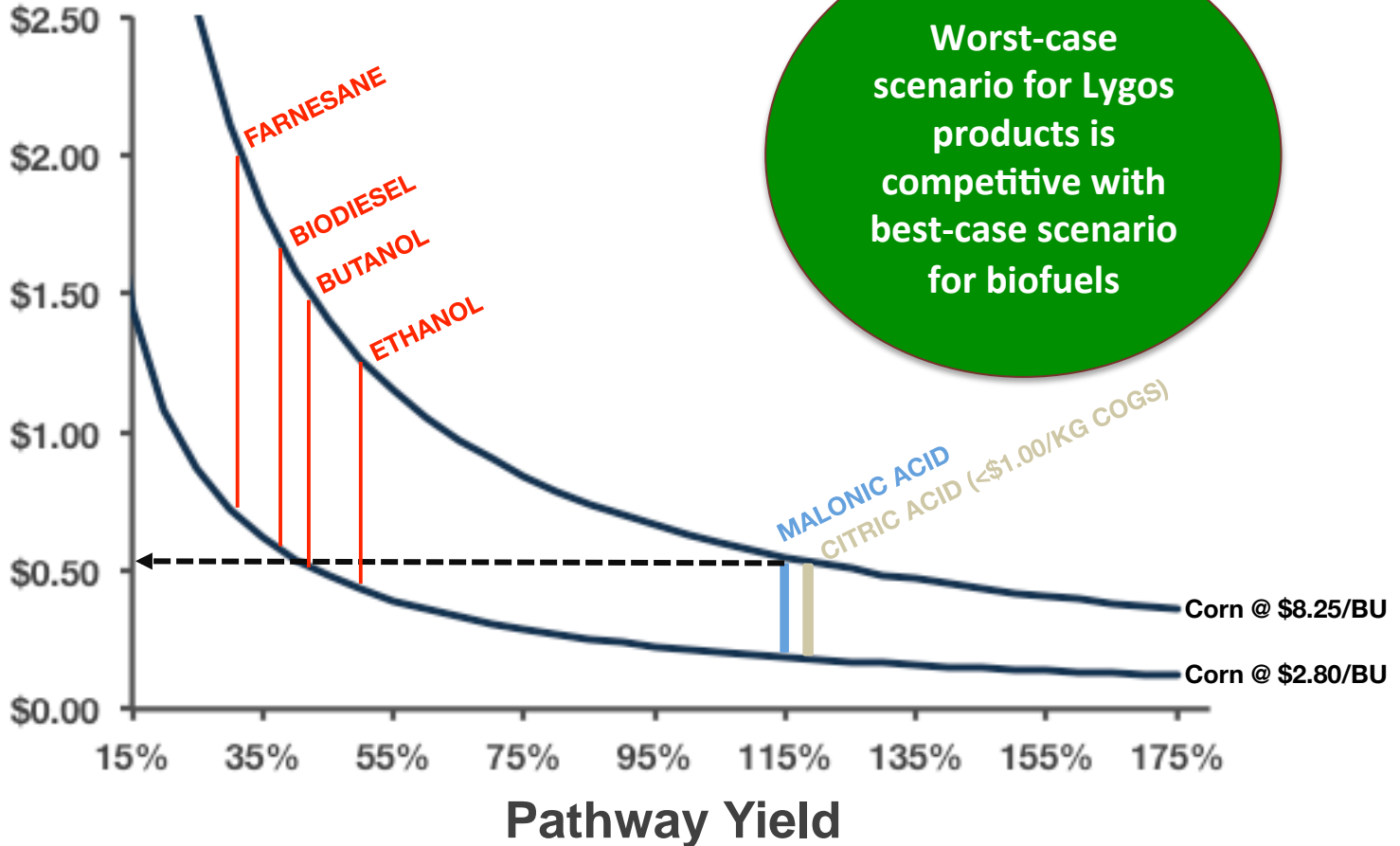
Berkeley  
UNIVERSITY OF CALIFORNIA

jbei  
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# Lygos Produces Bio-Advantaged Chemicals

**SUGAR COST  
(\$/KG PRODUCT)**



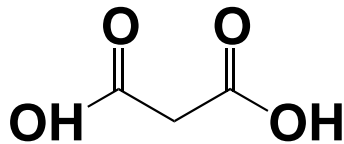
# Malonic Acid as a Bio-Advantaged Chemical

## Lygos' Biological Process



**SUGAR**

Malonic Acid



## Conventional Process



**PETROLEUM  
CYANIDE**

- ~\$250MM market today; \$1B opportunity
- Bio-production is less expensive than petro raw materials cost
- Bio-tech provides higher quality, better performing product

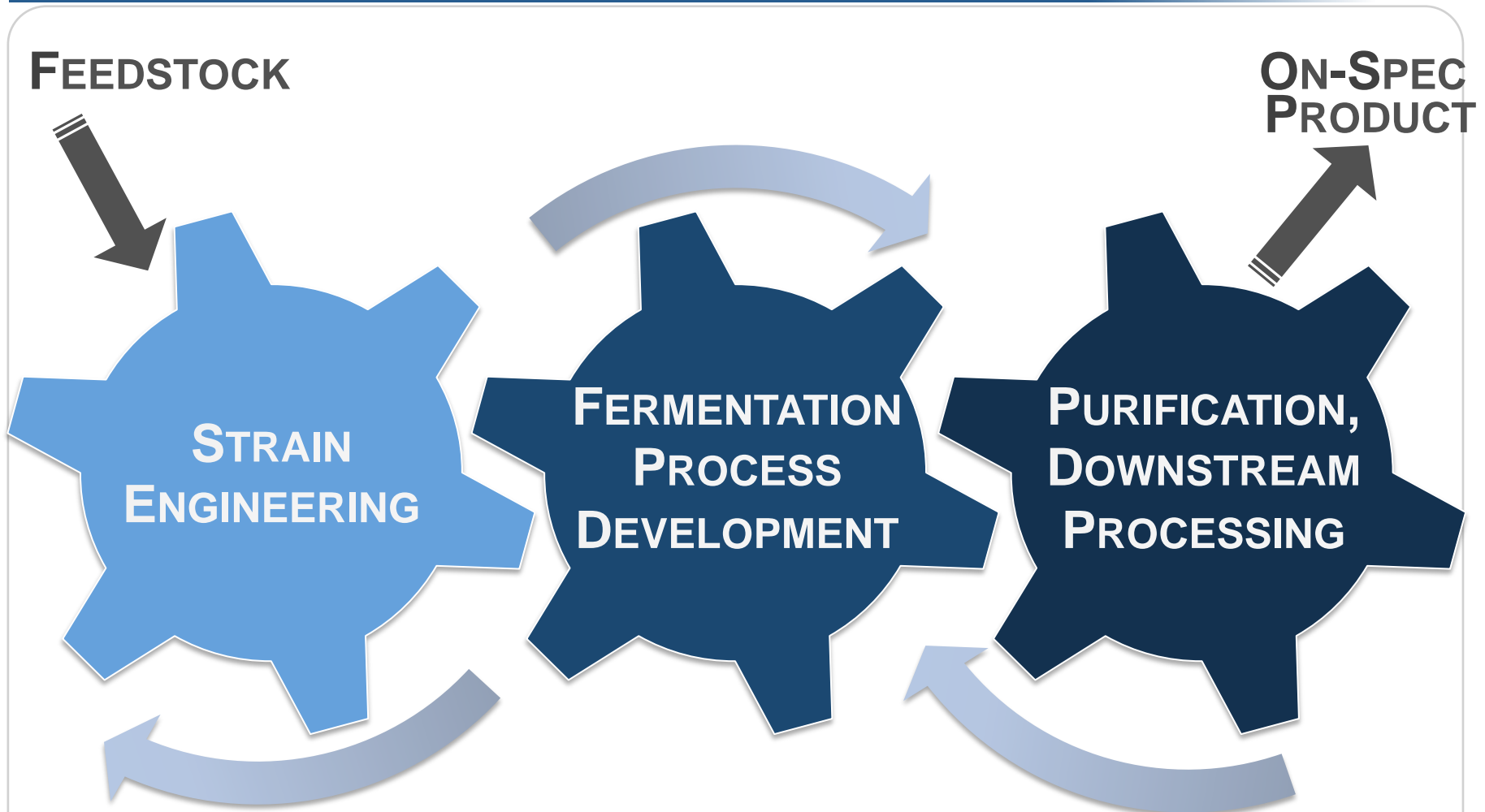
**Lygos advantages: cheaper, better, proprietary route**

# Commercializing Malonic Acid Today



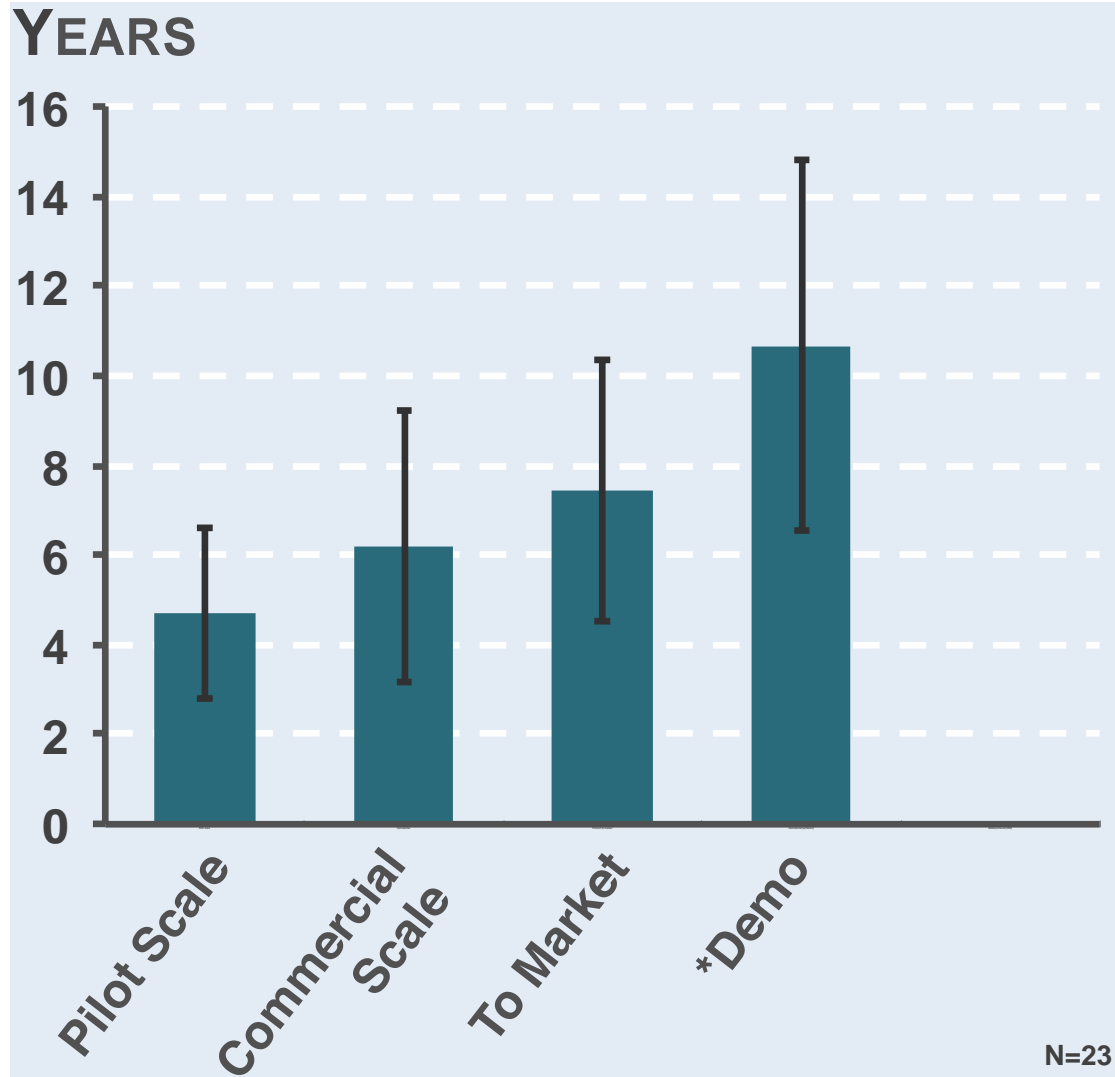
- Q1-2016:** Shipping kg samples of purified product (bench top scale)
- 2016:** Scaling integrated process
- Q4-2016:** Goal of shipping 1 MT purified product by end of year

# Design, Build, Test of the Integrated Process



**Strain engineering needs to be examined in the context of an integrated process**

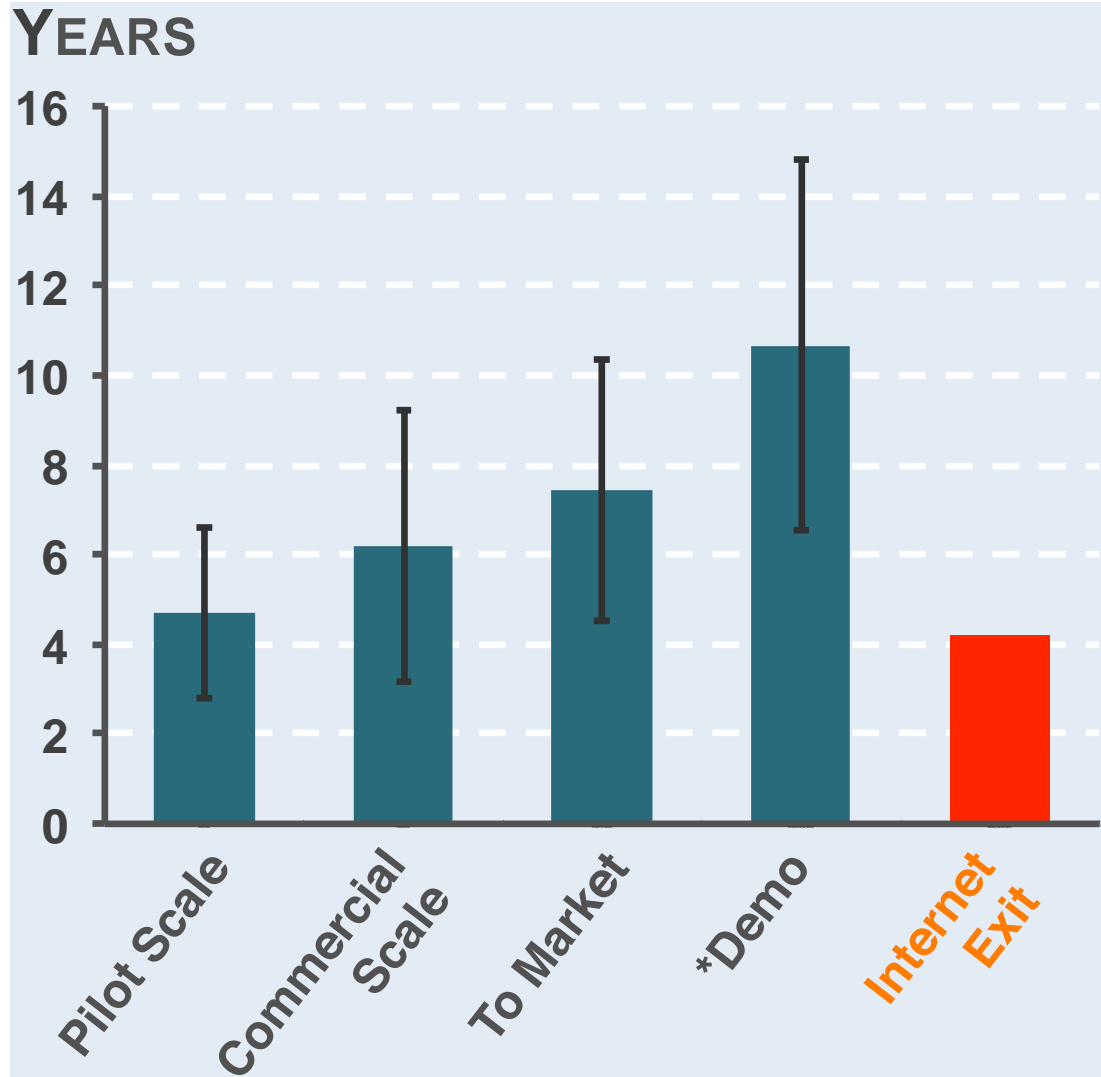
# DBTL Cycle Should Help Accelerate Commercialization



**Average time for a bio-based material or chemical to get to market is 7.42 years**

J. Allen, "Synthetic Biology: Applications and Lessons Learned in the Field of Bio-Based Materials and Chemicals." Lux Research (04/2015)

# DBTL Cycle Should Help Accelerate Commercialization



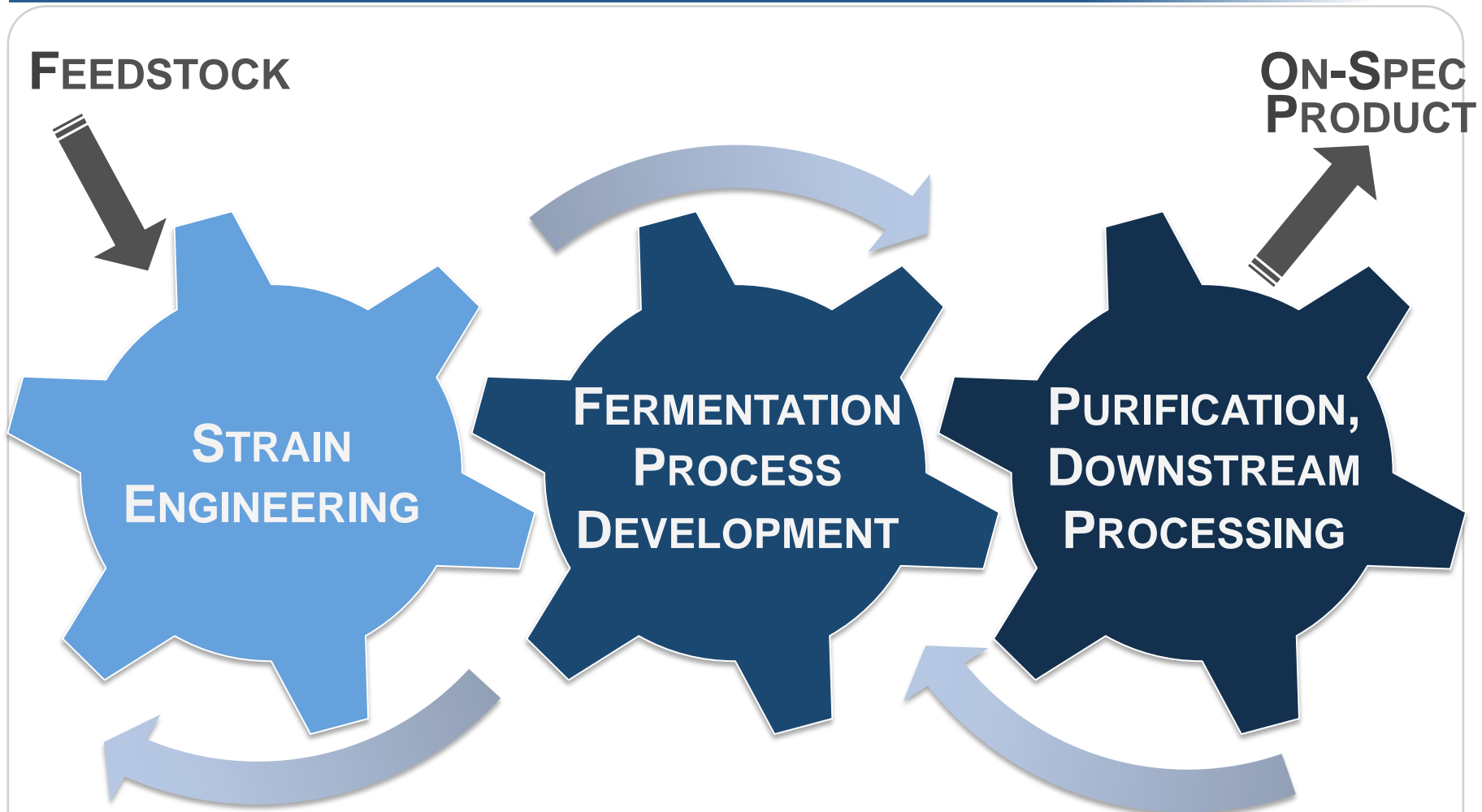
Average time for a bio-based material or chemical to get to market is 7.42 years

In 2013, the average time for an internet company to exit was 4.2 years

CB Insights Blog (November 7th, 2013)



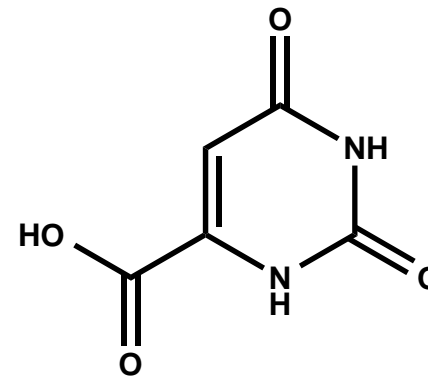
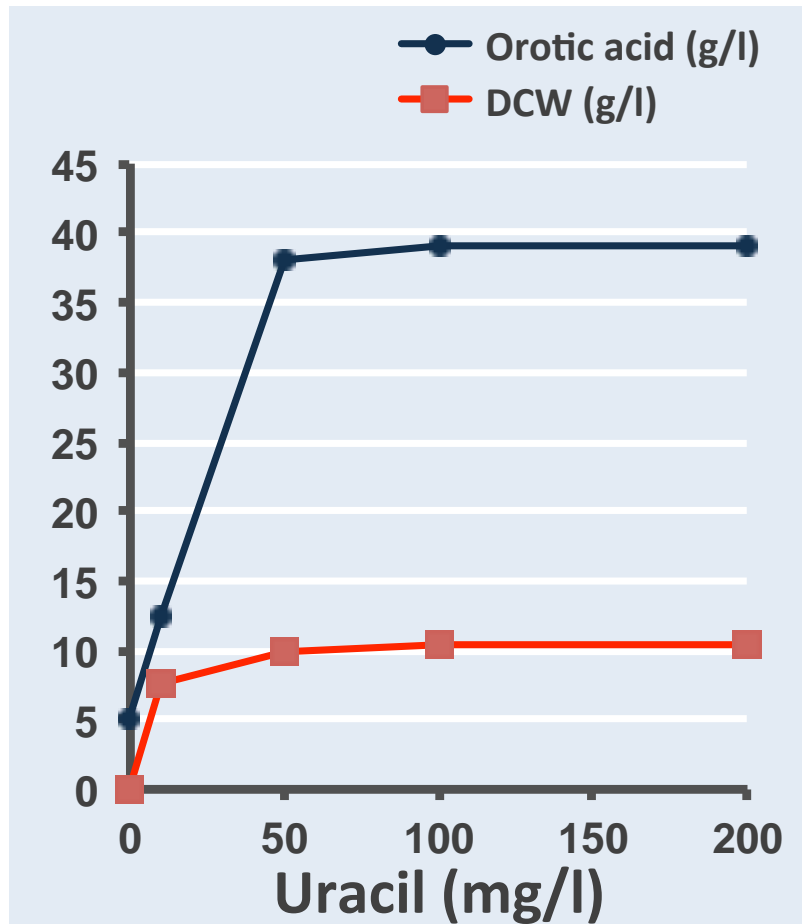
# Design, Build, Test of the Integrated Process



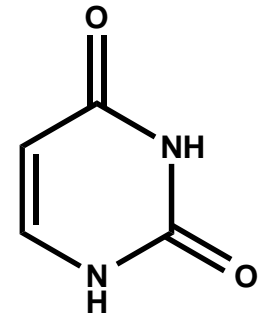
**Strain engineering needs to be examined in the context of an integrated process**

# Strain Engineering Strategy: Small Genotypic Changes with Large Phenotypic Outcomes

Example: one gene deletion (*ura3*) leads to uracil auxotrophy and orotic acid hyperproduction



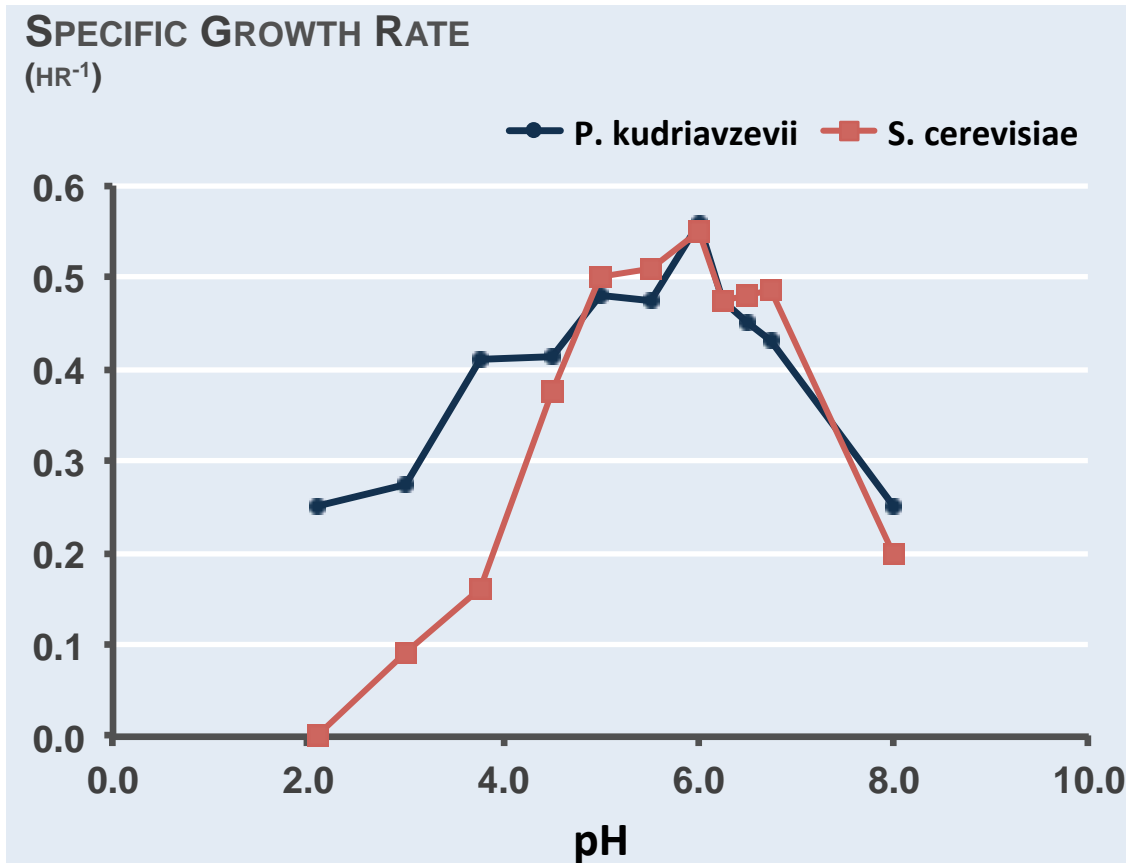
Orotic acid



Uracil

Adapted from Asahi, S et al. *BioSci. Biotech. Biochem.* 57:6 (1993)

# Fermentation Process Development: Use Production Hosts that Fit Into an Integrated Process

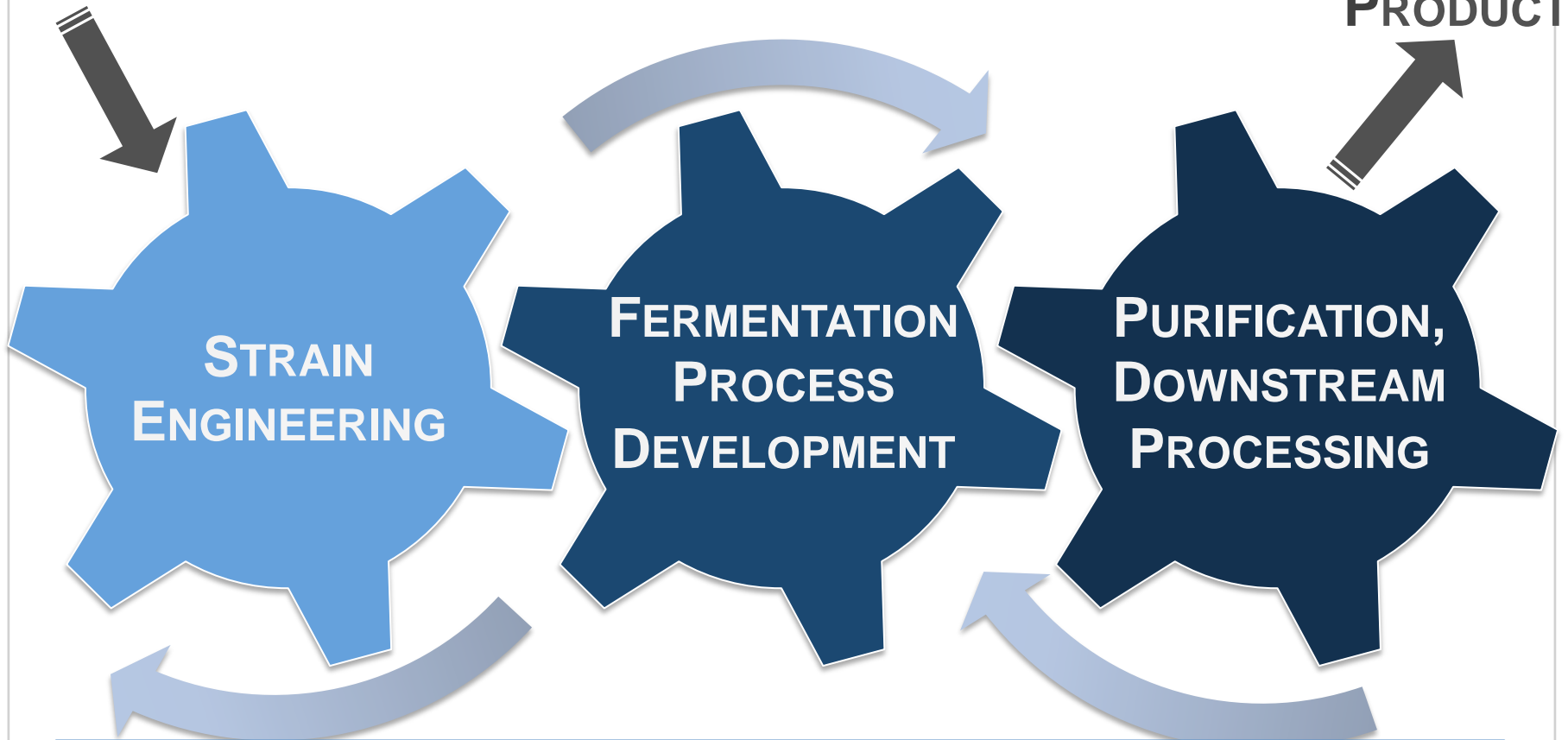


- *P. kudriavzevii* exhibits better pH tolerance than *S. cerevisiae*
- Reduces the amount of base required in a fermentation

# Design, Build, Test of the Integrated Process

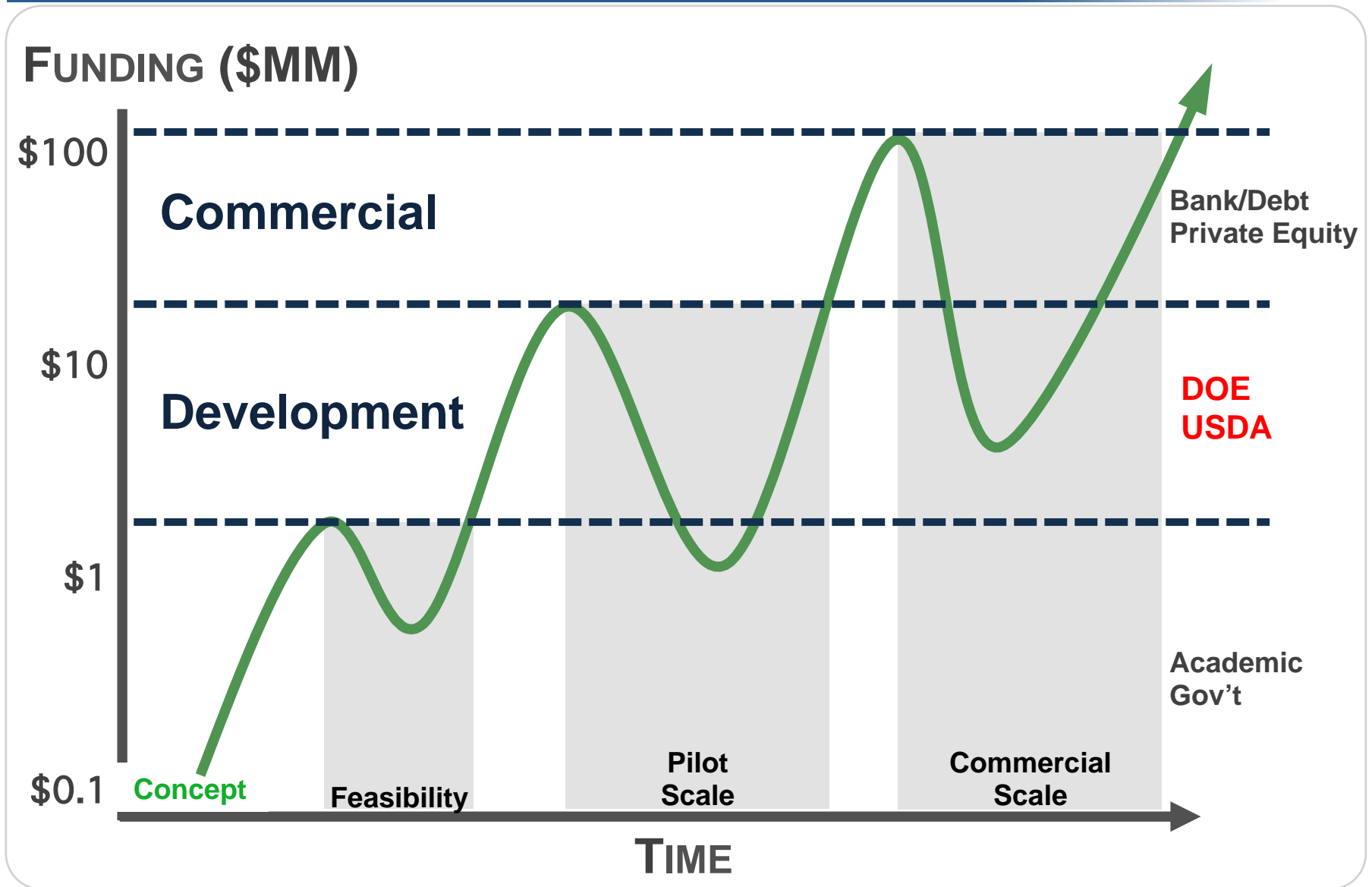
FEEDSTOCK

ON-SPEC  
PRODUCT

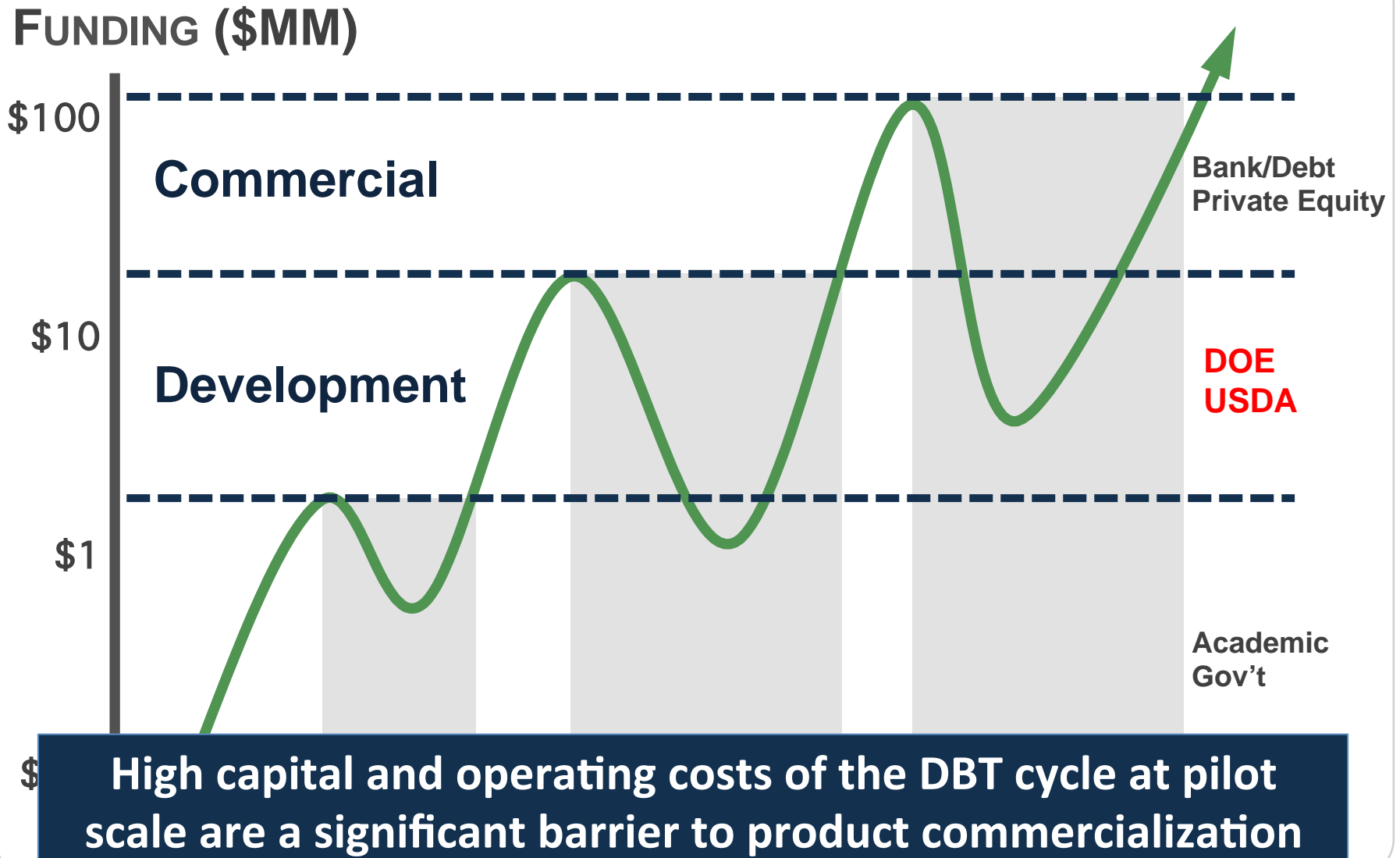


Does not address the key question, how to scale?

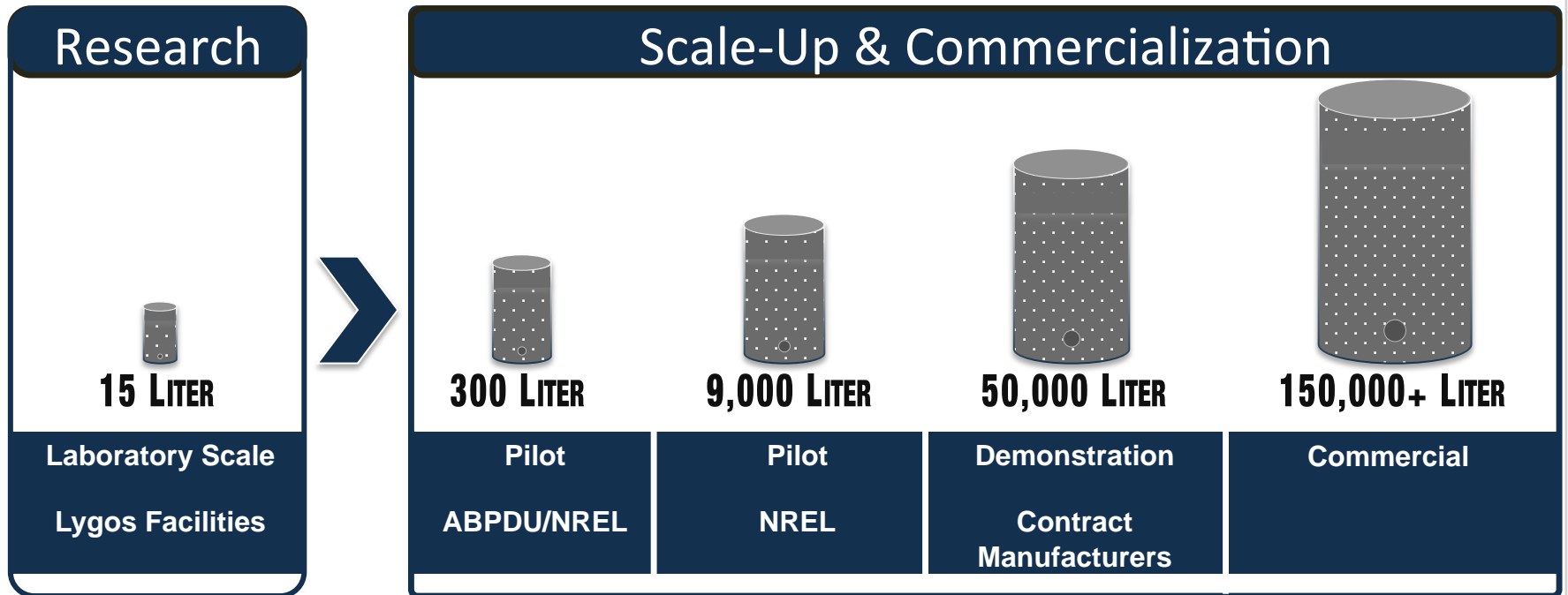
# Industrial BioTech Faces Three “Valleys of Death”



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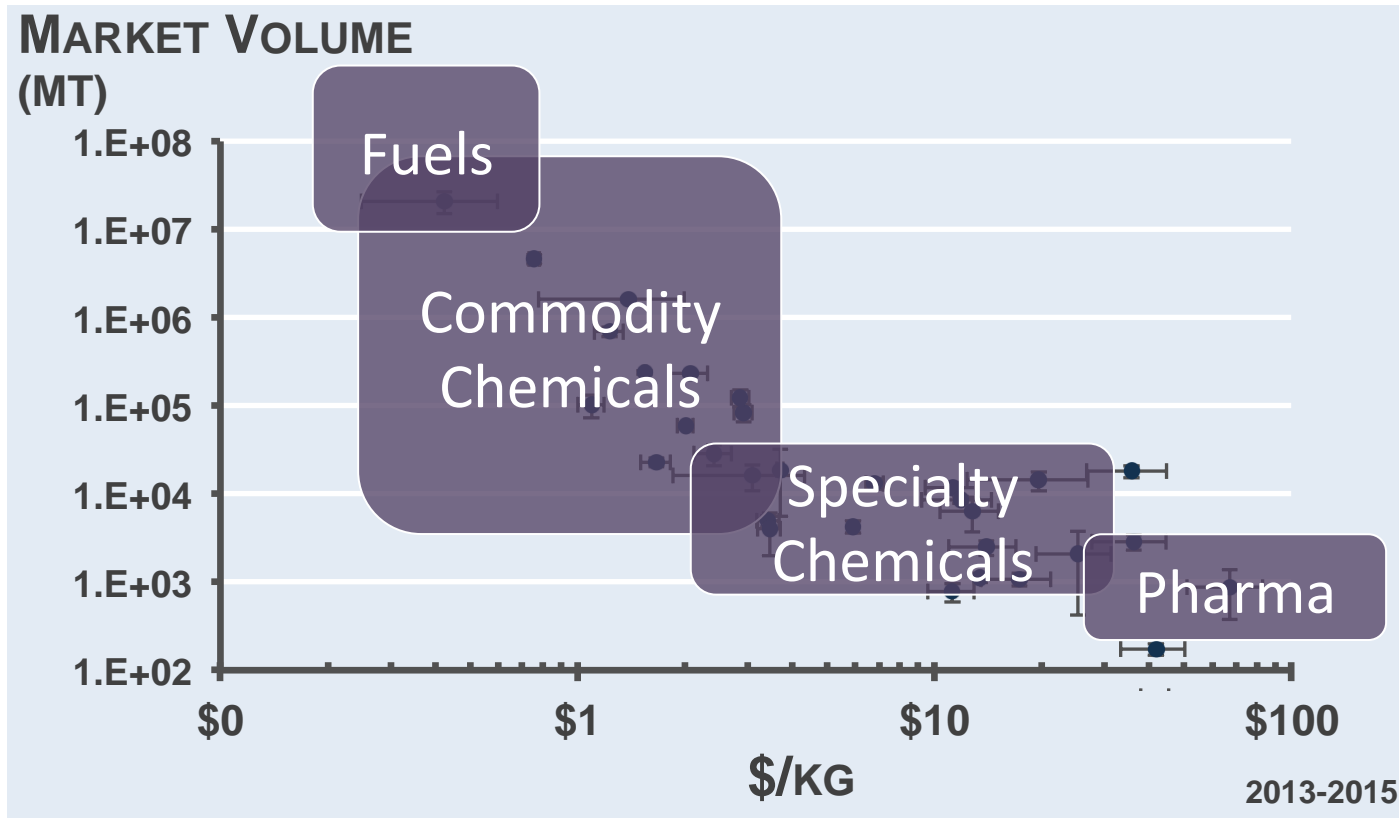


# Using Contract Manufacturing For Scaleup



- DOE small business voucher facilitates pilot scaleup to 9,000 liter fermenters
- High malonic acid price points allow for contract manufacturing and break-even economics

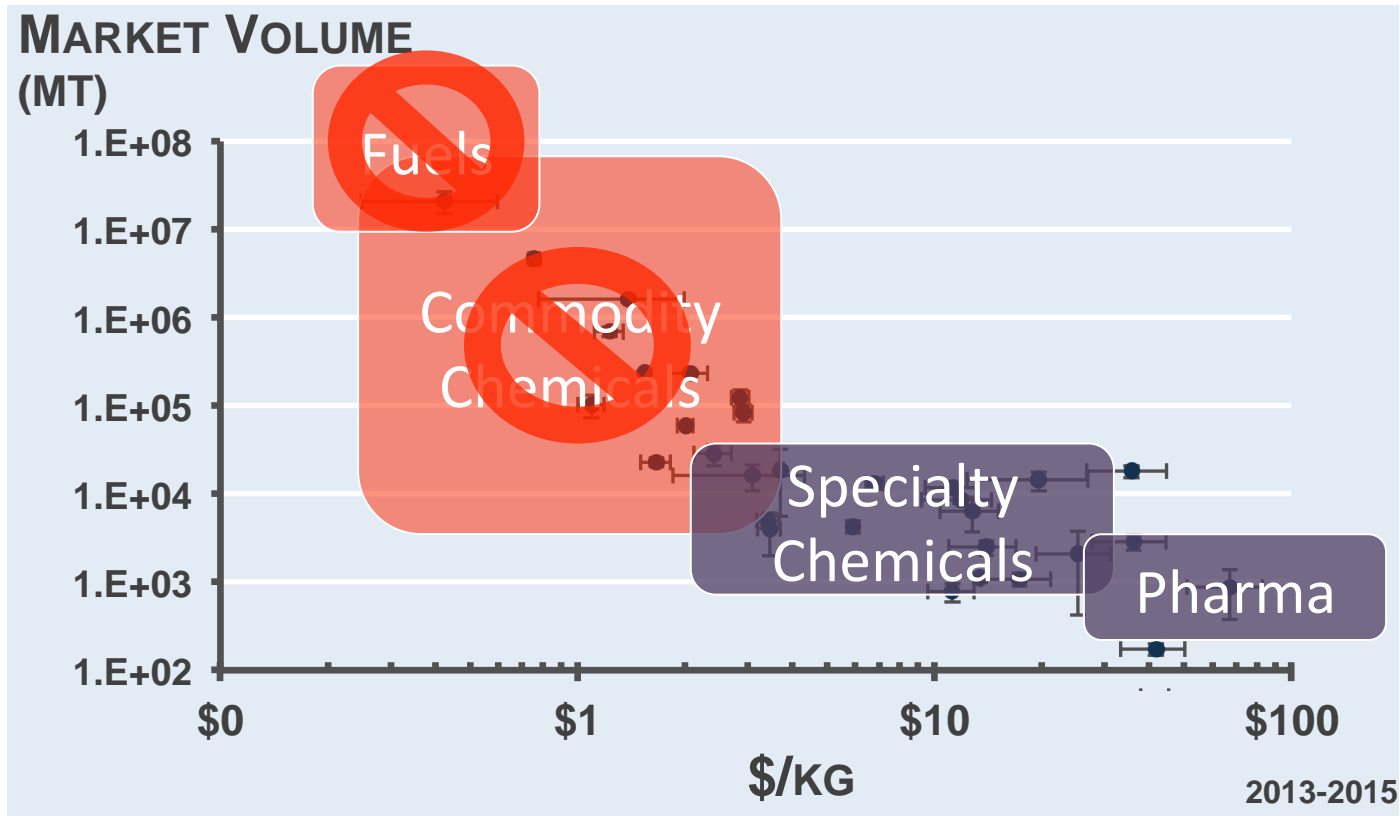
# Using Contract Manufacturing to Bridge Valley of Death



**High contract manufacturing costs preclude break-even production of fuels and commodity chemicals**



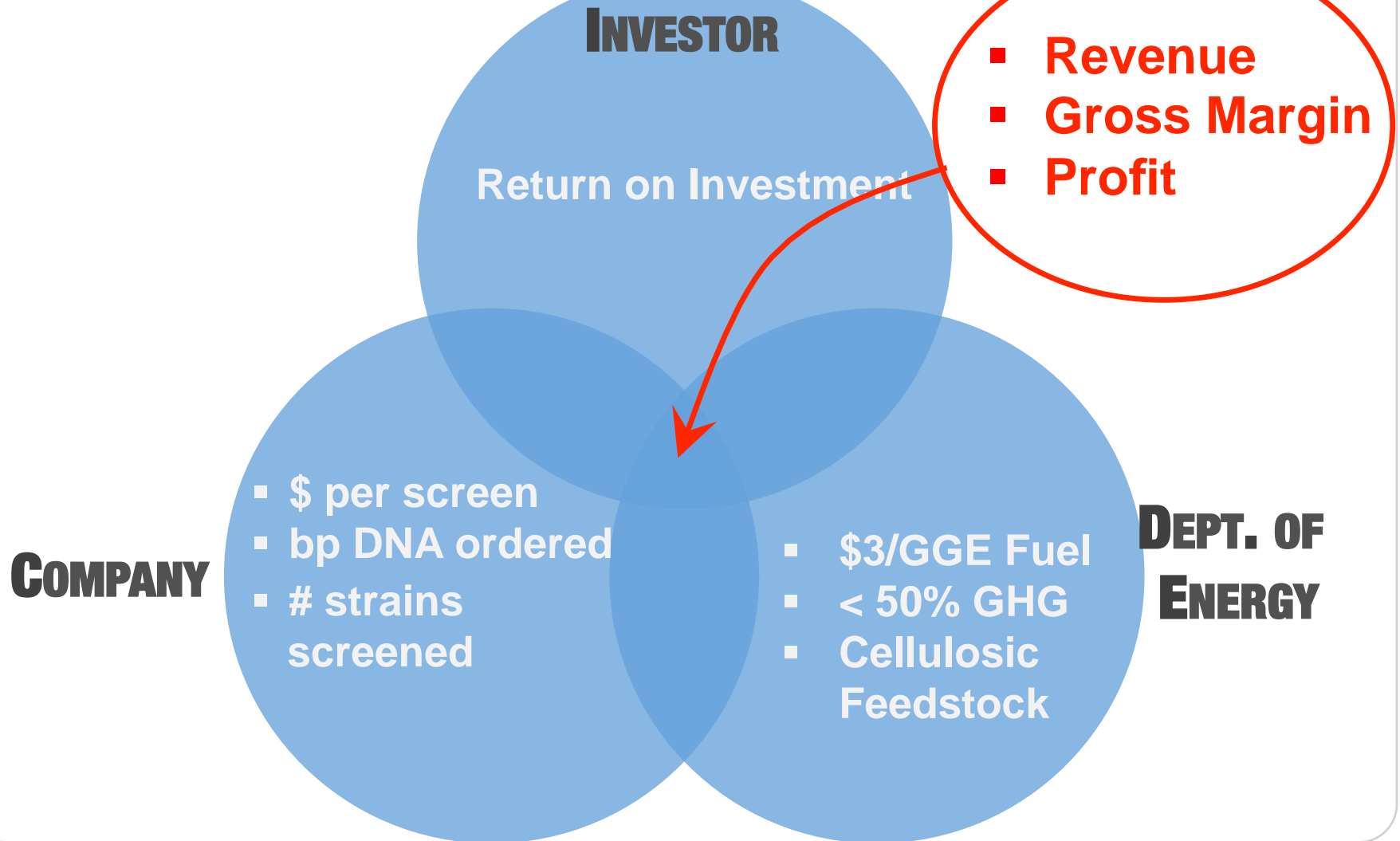
# Using Contract Manufacturing to Bridge Valley of Death



**Commercialization of fuels and commodity chemicals becomes more costly, time consuming, and difficult**

# DBTL Cycles: Need to Align Stakeholder Incentives

## Representative Stakeholder Metrics



# Thank You



Eric Steen  
David Melis  
Azadeh Alikhani  
Amanda Beverly  
Andrew Conley

Mario Ouellet  
Esther Kim  
Christine Carle  
Robert Wu  
Jacinto Chen

Daniel Blackburn  
Zach Hembree  
Desiree Srisavat  
Eric Gates