# Dyadic ®



### The Power of Nature, the Speed of Technology



### Safe Harbor Statement

Certain statements contained in this presentation are forward-looking statements. These forward-looking statements involve risks and uncertainties that could cause Dyadic's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by such forward-looking statements. Except as required by law, Dyadic expressly disclaims any intent or obligation to update any forward-looking statements.



# **Investment Highlights**



#### \* Patented Technology platform with vast potential

- C1 fungus-based expression system offers significant advantages over other microbial and cell culture-based systems
  - One-stop shop, same organism from discovery to production
  - Operating conditions, cost, scalability and yield

#### Risk-mitigated strategy to leverage platform into biopharmaceuticals

- Platform capabilities have been validated in industrial enzymes and biofuels through partnerships with key players
- Near-term potential to enter patent-protected markets in biopharmaceuticals through production of scientifically and commercially validated proteins, antibodies and vaccines

#### Experienced management & scientific teams; solid financial position



SAB

### **Management Team and SAB**



#### Scientific Advisory Board

Richard Lerner, M.D.	Chairman,
Carlos Barbas, Ph.D.	Advisor
Arnold Demain, Ph.D.	Advisor
Peter Punt, Ph.D.	Advisor
Arkady Sinitsyn, Ph.D.	Advisor
Cees van den Hondel, Ph.D.	Advisor

President of the Scripps Research Institute Scripps Research Institute, Chair Charles A. Dana Institute, MIT, Merck & Co. TNO Moscow State University Leiden University



### **Overview**

Patented and proprietary enabling biotechnologies for multi-billion dollar markets to develop biofuels, biotherapeutics, industrial enzymes and other bioproducts

#### \* "One-stop shop"

✤ Gene discovery to product manufacturing

#### ✤ Dyadic INSIDE<sup>®</sup>

 Cutting edge C1 technology to develop and manufacture diverse enzymes and proteins for existing and emerging industries



### **Partnerships**

- Important validation of technology platform
- Provide near-term cash flow to further advance platform capabilities
  - Leverages the capabilities and European reach of Dyadic Netherlands, Dyadic's R&D arm
- Expanding pipeline of potential licensees
- \* Non-exclusive license agreement with Codexis
  - Covers use of C1 expression system for large-scale production of enzymes in biofuels, chemical and pharmaceutical intermediate production
  - Upfront payment of \$10 million
  - Additional payments upon certain events



CODEXIS



### **Partnerships**

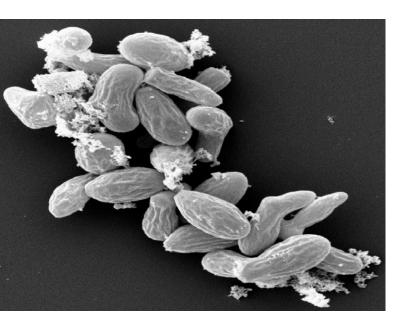


- Non-exclusive license agreement with Abengoa Bioenergy\*
  - Covers use of C1 expression system for large-scale production of enzymes for use in manufacturing biofuels, power and chemicals
  - \$10 million investment in Dyadic common stock
  - R&D program led to non-exclusive license agreement
  - ✤ Facility fees and royalties due to Dyadic upon commercialization
  - Currently focused on enzymes for lignocellulosic bioethanol production
  - ✤ Biomass Pilot Plant (US) in 2007 0.02 Mgal/yr capacity
    - ✤ Objective: competitive process with grain ethanol culture-based systems
  - ✤ Biomass Demonstration Plant (Spain) in 2008 1.3 Mgal/yr capacity
    - Objective: demonstrate commercial-scale process systems
  - ✤ Commercial Plant (US) in 2012
    - ✤ Objective: production at a gasoline competitive cost



### Patented Technology Platform Chrysosporium lucknowense\* (C1)

System for gene discovery, expression and protein production



A fungus isolated from alkaline soil in Eastern Russia

Platform for enzyme and protein production

- favorable fermentation characteristics
- high yield

#### Highly versatile

- can be used to produce a growing number of enzymes or proteins

\*Agency Response Letter GRAS Notice No. GRN 000292, CFSAN/Office of Food Additive Safety: The C1 strain was initially deposited with the International Depository of the All Russian Collection of Microorganisms of the Russian Academy of Sciences, and was assigned Accession Number VKM-3500D and classified as Chrysosporium luckowense based on morphological characteristics and subsequently reclassified as M. thermophilia based on genetic tests.



### **Dyadic Netherlands BV**

#### \* Research & Development arm of Dyadic Int'l.

- ✤ 16 employees 6 with Ph.D.'s
- Participation in a number of funded international projects

#### \* Located in Wageningen

- Wageningen University and Research Institutes
- ✤ Centre of excellence for Life Sciences research

#### Management Team

- Wim van der Wilden, Ph.D. General Manager
  - Former Director of R&D, Industrial Pharmaceutical Products Division Gist-brocades/DSM, TNO Quality of Life
- Jan Wery, Ph.D. Director, Science
  - Former Sr. Scientist, Netherlands Organization for Applied Scientific Research

#### www.dyadic.nl

### **Dyadic Netherlands BV**

#### \* Core competencies in:

- Enzymology
- Fungal High Throughput Robotic Screening\*
- ✤ Gene Expression
- Fermentation

#### \* Goal is:

- To apply technology to more industries and uses
- To manufacture vast quantities of diverse enzymes and proteins at higher yields and lower costs

\* Further development needed







### **Collaboration with Scripps**

- \* One of the world's largest and most reputable biomedical research organizations
  - Dr. Richard Lerner, President of Scripps, is the Chairman of Dyadic's SAB
- \* C1 genome sequencing and annotation 2005-2008
- Re-sequencing and re-annotation 2009-2010
  - Expanding knowledge of C1 genetics
  - Provides information and knowledge to improve C1 Technology Platform – to do more for less at higher yields.
  - Provides new product candidates and enzyme catalysts to improve manufacturing processes
  - Enter new markets

### **C-1 Technology Platform** From Promise to Product in 5 Steps: From Gene to Product in a Single Host Strain

### \* Gene discovery

- ✤ Access the full spectrum of biodiversity
- Robotic high-throughput screening

#### Sene expression

- Functional expression to identify genes
- Optimization

### \* Commercial Manufacturing

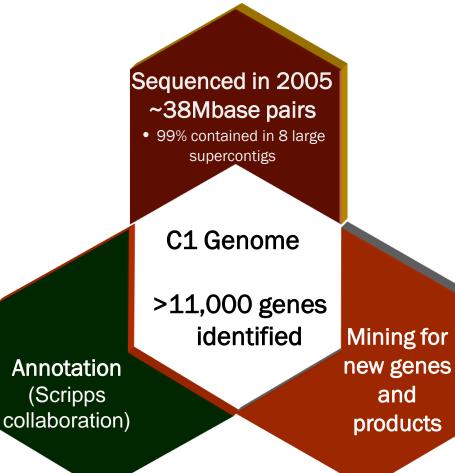
✤ Easy scale-up to 150,000L







### C1 gene discovery



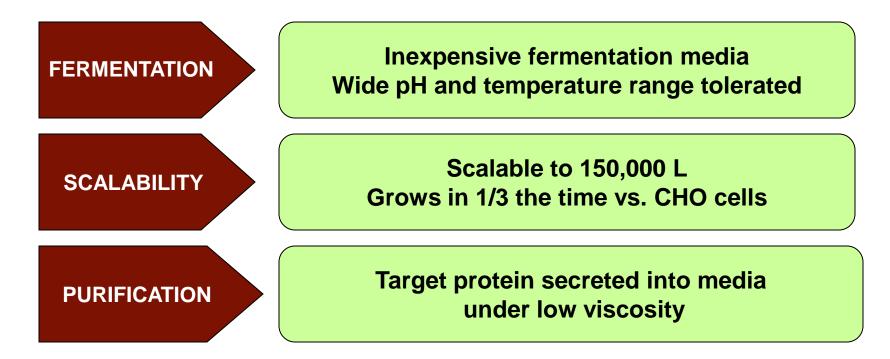
#### Over 200 genes encoding putative carbohydrate-active enzymes:

cellobiohydrolases endo-/exo- $\beta$ -glucanases endo-/exo-xylanases xyloglucanases, mannanases, arabinases, galactanases pectinases (pectin-/pectate lyases, polygalacturonases, etc.)  $\alpha$ -amylases, glucoamylases glycosidases ( $\alpha$ -/ $\beta$ -glucosidases,  $\alpha$ -/ $\beta$ -xylosidases,  $\alpha$ -/ $\beta$ galactosidases, α-Larabinofuranosidases,  $\alpha$ -/ $\beta$ mannosidases, etc.) ferulic acid esterases, cutinases, esterases, polyesterases





### High productivity-proven scalability



### Lower cost, greater yield Improved productivity



# **C1 Safety Profile: FDA GRAS**

### C1 strain

- Pathogenicity and toxicogenicity data: strain is non-infectious/no known toxins are produced
- Peer-reviewed scientific literature: No known pathogenicity

#### **C1-Enzyme preparation**

- In vivo feeding trials:
   14 day dose study in rats
   13 week subchronic rat study
- Genotoxicity testing: AMES bacterial mutagenesis Chromosomal aberration test Genetic mutation test

No mycotoxins found

- No adverse effects observed
- C1 Safety Profile: GRAS status acknowledged by the FDA



## **Strong Intellectual Property**

### \* 5 issued U.S. patents

- broad claims blocking use of C1
- 9 pending U.S. patent applications
- Large number of issued foreign patents and applications



### **Applications**

**Biofuels** Biopharma Agriculture **Chemicals** Food **Animal Feed Cosmetics Nutraceuticals** 





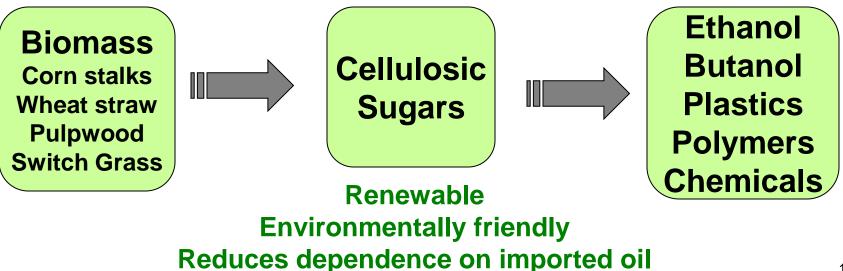






### **Energy Independence and Security Act of 2007**

Requirement to increase the volume of renewable fuel 9 billion gallons in 2008 36 billion gallons by 2022







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### **Biofuels: the Vision**

#### \* Development of proprietary enzymes for cellulosic bioethanol production

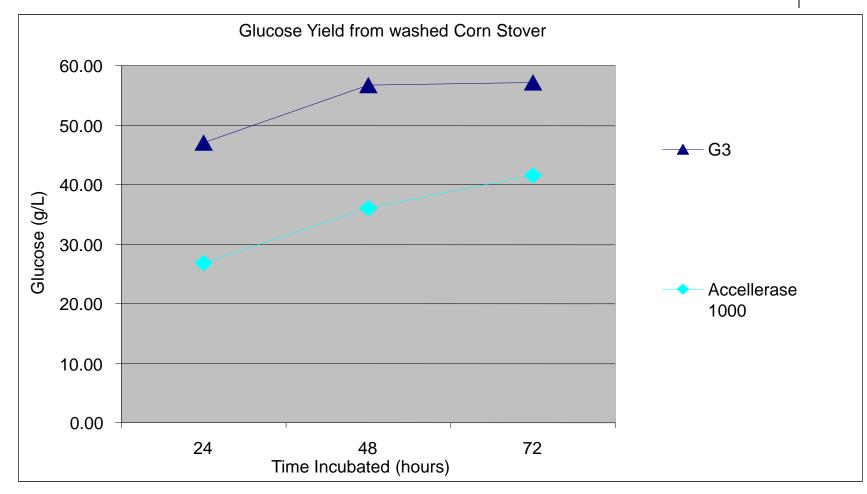
- Discovery and optimization of new enzymes
- Improve performance
- Lower costs

#### Performance of Dyadic's C1 Enzyme vs. Genencor's AccelleraseTM 1000\*

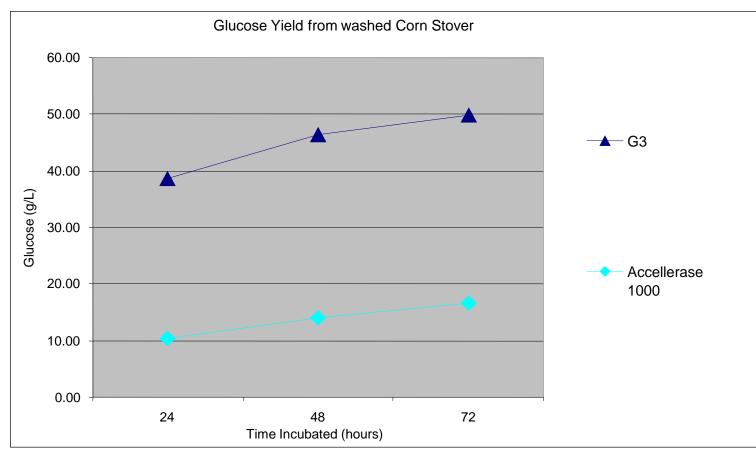
Enzyme Preparation	Protein dose (mg protein/g total solids) **	Temp (°C)	рН	Total Solids (% wt)	Glucose productivity (g/Lh <sup>-1</sup> )***	Relative Glucose productivity (%)
<b>Dyadic C1</b> (Chrysosporium sp)	20	50	5.0	10	0.86	97
	20	50	6.0	10	0.89	100
Accellerase™ 1000 (Trichoderma reesei)	20	50	5.0	10	0.73	82
	20	50	6.0	10	0.46	52

\*Substrate: pretreated hardwood, \*\*protein measured by BCA, \*\*\* 96h reaction

### C1 vs. Accellerase<sup>™</sup> 1000 at pH 5



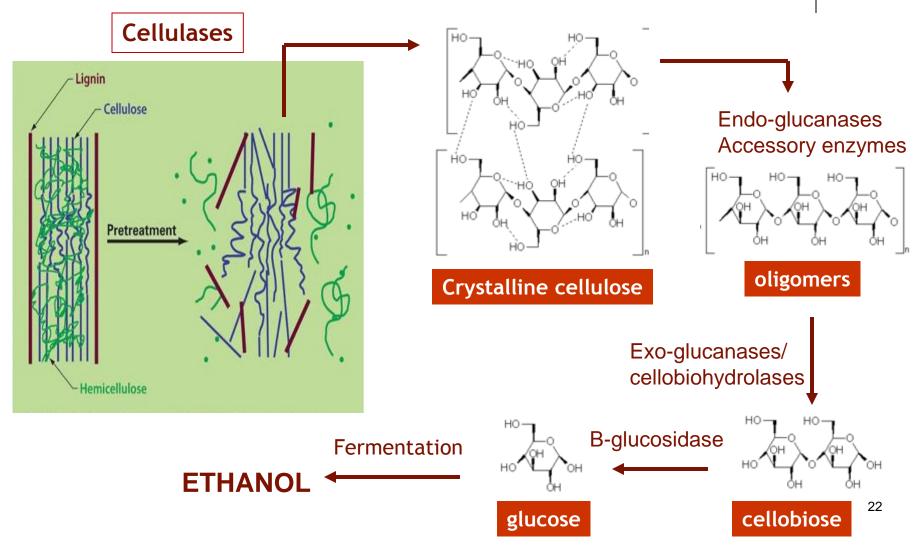
### C1 vs. Accellerase<sup>™</sup> 1000 at pH 6



#### Accelerase at pH 6 is ~ 50% less effective than at pH 5 C1 enzymes provide broader operating conditions



### **Enzymes for Biomass Saccharification**



### Comparison of C1 and Trichoderma



Comparison of the lignocellulolytic potential of C1 and *Trichoderma* reesei (the main industrial source for biofuel enzymes, e.g. Accellerase<sup>tm</sup>)

	<b>C1</b>	T.reesei**
Cellulases	~ 55	~ 35
Cellulose binding domains (CBM1)	~ 46	~11#
Xylanases	~ 11	~ 5
Arabinofuranosidases/arabinases	~ 14	~ 3
Esterases (Axe, Fae)	~ 10	~2#

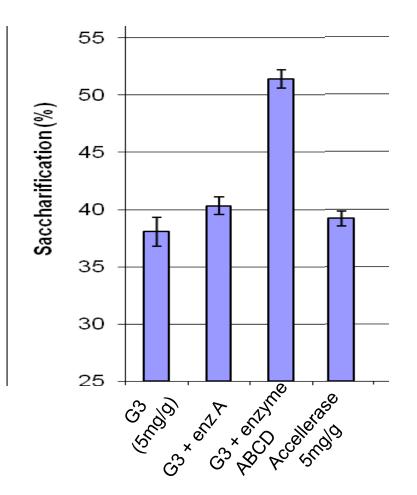
FIOM THE JGI DATADASE <sup>#</sup> Based on literature and JGI database searches

#### C1 is a rich source of lignocellulolytic enzymes!



### **C1 Strain Improvement**

#### Substrate: Pretreated corn stover



#### G3: An improved C1 strain for Biofuel Production

#### **Further improvements:**

- Addition of distinct C1 cellulases

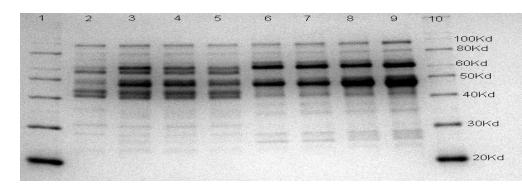
   to increase saccarification efficiency
   discovery of new enzymes (genomics)
   directed evolution of key single enzymes
- \* A single C1 strain producing optimized mix of enzymes
- Improve production yield from enzyme mixtures



### **Productivity Improvement**

$\bullet \bullet \bullet$

Ferm. No.	Strain	Medium Density	AzoCMC	BCA
			U/g	Protein
				g/l
EG2-17	UV18#100.f∆alp1	1x	728	n/a
EG2-18	EG2#65	1x	3,054	n/a
EG2-124	EG2#65	1.86x	3,507	68
EG2-125	EG2#257	1x	5,456	77
EG2-126	EG2#257	1.86x	6,457	86
14 Liters	EG2#257	1.86x	8,625	102



Protein production by optimized strain = 102g/L

# ~ 2X improvement over current strain



### **Commercial Enzymes**

- Dyadic has manufactured commercial enzymes since 1994
- Sales exceeded 1,300 metric tons through November 2009
- Over 50 products sold to customers in over 35 countries
- \* Excellent customer service and technical support
  - dedicated sales personnel in North and South America, Europe, Asia





Paper, pulp



#### Food, Brewing Animal Feed









### **Commercial Enzymes**

Food, Brewing, Animal Feed	Pulp and Paper	Textiles
CeluStarCL	FiberZyme LBL CONC	ROCKSOFT™ BioACE PLUS
Cellulase PLUS	FiberZyme PBL 100	ROCKSOFT™ BioACE 2X
Cellulase CP CONC	FiberZyme LBR	ROCKSOFT™ ACE P150
BrewZyme LP	FiberZyme PBR 100	ROCKSOFT™ Ultra L2500
$\beta$ Glucanase BP CONC	FiberZyme LDI	ROCKSOFT™ ACL CONC
Xylanase PLUS	FiberZyme PDI 100	ROCKSOFT™ ANTARCTIC LTC
Xylanase 2XP CONC		ROCKSOFT™ NCE L600
AlphaStar CO		ROCKSOFT™ NCE 2X
Protease AP CONC		ROCKSOFT™ NCE 3000
GlucoStar 400L		27



### **Biopharma Opportunity**

#### **\*** Therapeutic proteins and antibodies

- Over \$100 billion in sales
- Numerous patent expiries over the next decade
- No clear pathway for generics
- Opportunity to apply proprietary technologies to create differentiated products
  - Potential for efficacy improvements
  - New IP

### **\* CHO-based manufacturing system has limitations**

- ✤ Bottlenecks in development of master cell bank, scale up
- Other systems (plants, yeast) have faster growth cycles, but incorrect glycosylation



### **C1 for Protein and Antibody Production**

 High level of protein expression and secretion achieved

### \* To do:

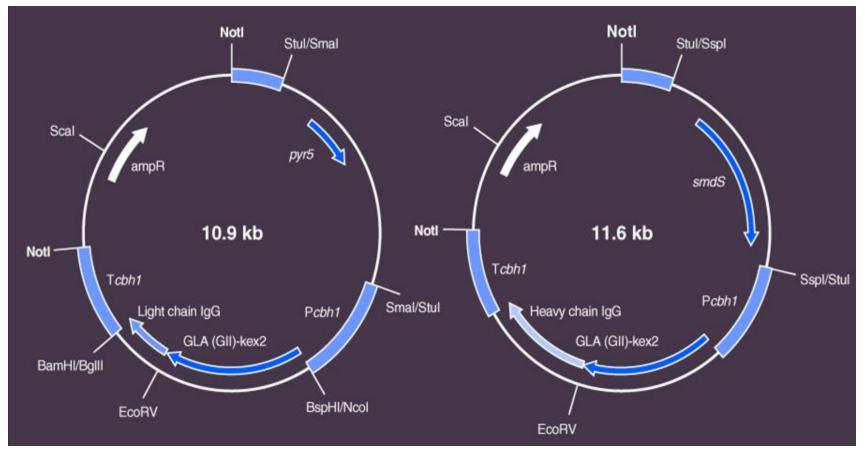
- Development of protease/cellulase KOs
- Promoter optimization
- Yield Improvements
- Glycoengineering
  - C1 glycoprofile is more similar to human than traditional fungi
  - Further humanization required
  - Unglycosylated proteins can be made

# Advantages over GlycoFi's Pichia (acquired by Merck)

 Safety: Agency Response Letter GRAS Notice No. GRN 000292 (Received September 29, 2009)

### **Antibody Production in C1**

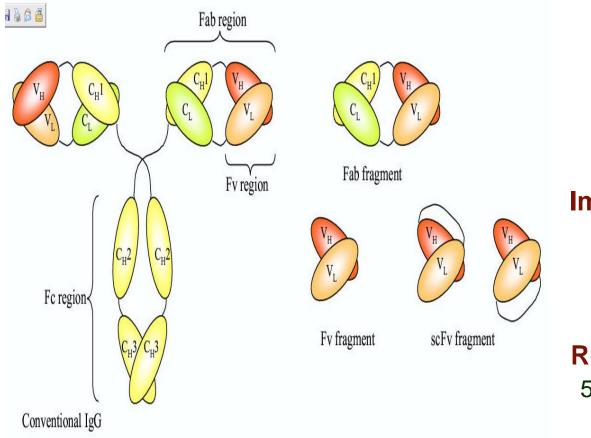
**Construction of C1 Strains Expressing Full-length Human Antibodies** 







### **Antibody Production in C1**



#### Antibody production level

>1 g/l levels reached in initial strain/process optimization

#### Improved copy number host strains

2-fold increase (>2 g/l) in production reached

### Room for improvement

5-10 g/l achievable in about 1 year

# **Vaccines: Opportunity**

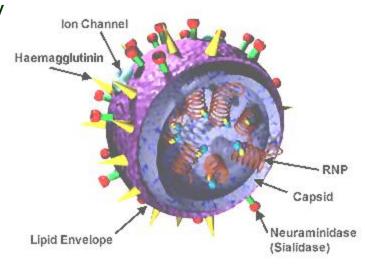
- \* Vaccine sales exceed \$10 billion
- Dominated by seasonal flu vaccine
  - Made in chicken eggs, using old technology
  - ✤ Six month production cycle

### \* Opportunity to manufacture in Cl

Improve cycle time, yield and cost

### Non-flu vaccines

Improve protection by altered glycosylation



#### **INFLUENZA VIRUS**



# Financial Summary (as of 9/30/09)

- Shares Issued and Outstanding
- \* Cash Position (9/30/09)
- \* Debt
- \* Total Revenue (Q3, 2009)
- \* Total Revenue (1/1/09-9/30/09)

30.2 million \$9.2 million \$1.4 million \$2.1 million \$19 million\*

\* includes license revenue, product revenue and research revenue. Revenue will vary significantly quarter to quarter based on Dyadic's ability to secure additional partnerships.

### **Comparable Companies**

Company	Sector	Ann. Rev.	<b>Acquisition Price</b>
Glycofi	Biopharma		\$400M
0	Center	Area Dese	Maluation
Company	Sector	Ann. Rev.	Valuation
Crucell	Biopharma	\$360M	\$1.7B
Protalix	Biopharma	\$0M	\$603M
Codexis	Enzymes	N/A	Private co.
Verenium	Enzymes	\$69M	\$48 <b>M</b>
Maxygen	Biopharma	\$29M	\$223M





# **Key Milestones**

☑Received \$10 million equity investment and entered into an R&D collaboration with Abengoa Bioenergy

☑Non-exclusive license agreement with Abengoa

- Entered into a non-exclusive license agreement with Codexis
- ☑Received \$10 million upfront payment from Codexis
- Bioenergy
- ☑ Received GRAS notice from the FDA
- ✓Extended collaboration with Scripps
- R&D funding private and public sources
- Additional license agreements, partnerships for biofuels, industrial enzymes, feed, food, cosmetics, nutraceuticals, biopharmaceuticals
- Receipt of milestone fees, facility fees and royalties existing agreements



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#### Experienced management & scientific teams; solid financial position