The C1 Technology Platform

Making Healthcare Accessible & Affordable

NASDAQ: DYAI

Roth Investor Presentation – March 17, 2020
Certain statements contained in this presentation are forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934, including those regarding Dyadic’s expectations, intentions, strategies and beliefs pertaining to future events or future financial performance. Actual events or results may differ materially from those in the forward-looking statements as a result of various important factors, including those described in Dyadic’s most recent filings with the SEC. Undue reliance should not be placed on the forward-looking statements in this press release, which are based on information available to us on the date hereof. Dyadic assumes no obligation to update publicly any such forward-looking statements, whether as a result of new information, future events or otherwise. For a more complete description of the risks that could cause our actual results to differ from our current expectations, please see the section entitled “Risk Factors” in Dyadic’s annual reports on Form 10-K and quarterly reports on Form 10-Q filed with the SEC, as such factors may be updated from time to time in Dyadic’s periodic filings with the SEC, which are accessible on the SEC’s website at www.dyadic.com.
Dyadic Investment Thesis

Proprietary Technology - C1 Fungal Gene Expression Platform - Broad Applications

Recent Nasdaq Listing; Compelling Valuation

Funded On-going R&D Collaborations with Top Tier Pharm

Experienced Board Members and Management Team

Strong Balance Sheet

Proven Technology for Industrial Use

- US$37.2M cash & equivalents\(^1\)
- No Debt or Warrants

\(^1\) As of September 30, 2019, incl. accrued Interest

Success in Industrial Use

Over Two Decades Of Biotechnology Experience

Sold Industrial Biotech Unit to DuPont for $75M in 2015

April 17, 2019

Up-listed on Nasdaq Capital Markets

\(\text{DYADIC INFORMATION} \ 3\)
Dyadic Highlight

- Ticker: NASDAQ: DYAI
- Share Price: $3.31
- 52 Weeks Range: $3.31-$8.00
- Market Capitalization: ~$90 million
- Shares Outstanding: ~27.7 million
- Insider Ownership Percentage: 30.3%
- Debt/Warrants: None
- Cash and Investment Grade Securities: ~$37.2 million

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1 As of 3/17/2020
2 As of 9/30/2019, including Francisco Trust
3 Based on 9/30/2019 balance, incl. accrued interest
Dyadic Overview

HQ: Jupiter, FL
BD&L: London
R&D: Valladolid
R&D Management: Budapest
R&D: Helsinki

20+ YEARS EXPERIENCE IN BIOPHARMA BD&L AND FUNGAL GENE EXPRESSION PLATFORM R&D
M. Emalfarb  
Founder, CEO

More than 20 years’ finance and accounting experience, including technical accounting, SEC reporting, acquisition, and capital market consulting to large banks and multinational public companies. 
MBA and MS in Accounting from SUNY Buffalo and CPA in New York State.

P. Rawson  
Chief Financial Officer

Inventor of 25+ U.S. and foreign biotechnology patents related to Dyadic’s proprietary C1 fungus. 
Formation of several strategic research and development, manufacturing and marketing relationships with U.S. and international partners since founding the company in 1979.

R. Tchelet  
Chief Scientific Officer

More than 15 years of experience in research and pharmaceutical industry. Previously, CTO of Biotech at the API Division of TEVA Pharmaceuticals and founder and Managing Director of Codexis Laboratories Hungary. 
Ph.D. in Molecular Microbiology and Biotechnology from Tel Aviv University in 1993 and Postdoctoral as an EERO fellow at the Institute of Environmental Science and Technology (EAWAG) in Switzerland.

M. Jones  
Chief Commercial Officer

More than 20 years life science and BioPharma industry leadership as well as Private Equity deal making advisory experience incl. a founding member of Concept Life Sciences. Senior roles held with Lonza, Bain, Ricerca BioSciences, MDS Pharma Services, Alkermes and GlaxoSmithKline.

Mr. Jones leads Dyadic’s Commercial deal making BD and Licensing.
Dr. Bose worked at Pfizer for 34 years and held leadership roles within bioprocess development and clinical manufacturing and is widely recognized as a Key Thought Leader in the biopharmaceutical industry.

Dr. Bose is a Member of the US National Academy of Engineering. Additionally, he was elected Fellow of AIChE, American Chemical Society and American Institute for Medical and Biological Engineering.

Dr. Buckland worked at Merck for 29 years where he served in a number of senior R&D leadership roles focusing on fermentation and bioprocess development and the commercial manufacturing of biologics and is widely recognized as a Key Thought Leader in the biopharmaceutical industry. Currently, Dr. Buckland is the Executive Director, NIIMBL (National Institute for Innovation in Manufacturing Biopharmaceuticals).

Dr. Buckland is a Member of the prestigious US National Academy of Engineering. In addition, he is a Fellow of the American Institute of Medical and Biological Engineering (AIMBE) as well as of University College, London.

Mr. Tarnok (Dyadic chairman) spent the majority of his career at Pfizer and is a seasoned finance and operational executive with extensive experience in the pharmaceutical industry. Currently also serves on the Board of the Global Health Council, and Ionetix, Inc. Prior Board service includes Keryx Biopharmaceuticals, Inc., where he also served as Chairman of the Board.
2019 Corporate Achievements and Milestones

Corporate Achievements
- Form 10 effective on February 12, 2019
- Initiated trading on Nasdaq on April 17, 2019
- Dyadic stock was added to the Russell Microcap® Index in May 2019

Serum Institute of India Collaboration Announced May 7, 2019
- Collaboration to express and manufacture in C1 up to 12 antibodies and vaccines
- Research funding, milestone payments, royalties/licensing

Four Additional Proof-of-Concept Collaborations with Top Pharma Companies
- Centered on various classes of proteins, mAbs, and vaccine antigens
- Following 9 collaborations in 2018, including those with Sanofi-Aventis, and the Israeli Institute of Biological Research (IIBR).

Two Sublicensing Agreements
- Luina Bio/Novovet: with equity stake and royalties to sub-license C1 platform to develop biologic vaccines and drugs for companion animals
- Alphazyme: with equity stake, milestone payments, and royalties to sub-license C1 gene expression platform for reagents in therapies or diagnostics

One Fully Funded Collaboration with a Leading Animal Health Company

Two Research Licenses:
- Expanded relationship with one leading pharma company – an existing collaborator
- University of Iowa
Biopharmaceutical Market Overview - The Opportunities

**TWO OF TOP FOUR ANIMAL HEALTH CO’s**
ZAPI, BDI, NOVOVET and others
Recombinant vaccines for animal health
Market size – $8.7 Billion by 2022

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**Sanofi, and others**
New Biologics
mAbs, Bispecifics, Fc-Fusions
BioPharmaceutical Market size – $319 Billion by 2021

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**Cimzia, Opdivo®**
Biosimilars / Biobetters (non-Glyco. and Glyco Proteins.)
Global Market size – $69 Billion by 2025

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**ZAPI, IIBR and Coronavirus**
Vaccines and drugs for Pandemic and Epidemic zoonotic diseases and biologic threats

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**Serum, and others**
Recombinant vaccines and drugs for human health
Market size – $66.5 Billion by 2027

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**In-house projects**
Primary and secondary metabolites
AAV Viral Vectors

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1. Source [https://tinyurl.com/y544yxq7](https://tinyurl.com/y544yxq7)
2. Source [https://tinyurl.com/yyurkcm1](https://tinyurl.com/yyurkcm1)
3. Source [https://tinyurl.com/yxtfsm6y](https://tinyurl.com/yxtfsm6y)
4. Source [https://tinyurl.com/y2qq78ss](https://tinyurl.com/y2qq78ss)
5. Evaluating Next Steps
C1 Gene Expression Platform
C1 – *Myceliophthora thermophila*

C1 is a thermophilic fungus, *Myceliophthora thermophila*, originally isolated from alkaline soil in Russia.

Dyadic and its licensees invested several hundred million dollars to turn C1 into an industrially proven gene expression platform.

- Low cost, high yield, scalable, robust and stable system with improved downstream purification benefits
- C1 genome fully sequenced and annotated
- C1 received a Generally Recognized As Safe (GRAS) designation from the US FDA (2009)

Proprietary & patented genetic elements (tool box) for use in engineering C1 strains

Clear demonstration that C1 can speed development & lower costs of biopharmaceutical production
Dyadic built an industrial enzyme business, and licensed the C1 technology platform for industrial uses to Abengoa, BASF, Codexis/Shell and others:

- Generated >$100 mm in enzyme product revenues from customers in 35 countries
- Received > $30 mm in cash payments for non-exclusive licenses

Sold the Industrial Biotech Business to DuPont for $75 mm on 12/31/2015

We now apply the powerful C1 gene expression workhorse technology to human and animal therapeutic products
C1 – The Science

High Purity of target protein secreted
- Greater retention of target secreted protein through downstream processing
- Requires only low cost synthetic media
- No Viruses which simplifies processing compared to CHO
  - No Low pH viral inactivation
  - No virus nanofiltration

Shorter Development & Production Cycle
- Develop g/l/d C1 cell lines in 15 weeks
- From seed flask to fermenter
  - Savings of nearly 10 -14 days vs CHO
- Develop g/l/d C1 cell lines in 15 weeks
- Fermentation Cycle time 4-7 days
  - 1/2 to 1/3rd the time of CHO

Unique Morphology
Translates into better growth conditions
- Higher yields of secreted protein
- Lower viscosity

Wide operating conditions for pH and temperature
- At scales ranging from laboratory shake flasks to 20,000l tanks and above
- C1 has received GRAS (Generally Recognized as Safe) designation from FDA and is considered fit for human consumption
How Dyadic Leverages C1 Advantages for Biologics

- High productivity -
- Advanced genetic tools (Efficient transformation) -
  - Efficient secretory system -
  - Low viscosity -
- Wide range of fermentation conditions -
  - Fast growing -
- Grow on simple defined media -
- Can tolerant high glucose concentration -
- Easy scaling up (was scaled up to 500m³) -

Efficient vast screening system for drug discovery
Fast development timeline for Biologics
Simple fermentation process in stainless steal bioreactors
Success in Single use reactors
Low cost of USP & DSP

Growing on 24 or 96 MTP
Generic Process Flow Chart for C1 (12 – 14 days) (*)

- Pre-inoculum: Mycelium activation
- Seed train: inoculum expansion in flask
- Inoculum expansion - bioreactors
- Production bioreactor
- Passage 1 plate
- Passage 2 flask

- N-3 ~1.6L scale
- N-2 ~40L scale
- N-1 ~1000L scale
- N ~12,000L scale

- 1 – 1.5 days
- 0.75 – 2.5 days
- 5 days
Generic Process Flow Chart for CHO (41 – 54 days)

18-28 d

9-12 days

14 days

Seed train: inoculum expansion

Passage 1
Passage 2
Passage 3
Passage 4
Passage 5
Passage 6

Inoculum expansion - bioreactors

N-3 ~80L scale
N-2 ~400L scale
N-1 ~2,000L scale

Production bioreactor

N ~12,000L scale
C1 Can Operate Successfully in Single Use Bioreactor

C1, a filamentous fungi, produces Certolizumab in Single Use bioreactors with the same performances as Stainless Steel Bioreactors.

The productivity of 9.2 g/l is virtually identical to the productivity achieved in the Stainless Steel Bioreactor control that was based on an earlier C1 Certolizumab strain and process. The current yield in SSB is 14.5 g/l in 7 days fermentation.

Results between batches are consistent, showing the robustness of the technology.

Certolizumab production in SUB (g/L)

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Single Use Bioreactor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial medium: 25L</td>
<td></td>
</tr>
<tr>
<td>Final broth: 32kg</td>
<td></td>
</tr>
<tr>
<td>d02 controlled by air flow</td>
<td></td>
</tr>
<tr>
<td>Pure oxygen addition.</td>
<td></td>
</tr>
<tr>
<td>Titer / Time</td>
<td>9.2 g/L at 112 hrs</td>
</tr>
<tr>
<td>Productivity</td>
<td>2.0 g/L/day</td>
</tr>
</tbody>
</table>

Equipment: 50L XDR-50MO
Single Use GE bioreactor
Product protein: Certolizumab
C1 Applied to Production of Therapeutic Proteins
C1 Gene Expression System is a Versatile “Workhorse”

Impressive Yield and Purity Demonstrated for Therapeutic Proteins

<table>
<thead>
<tr>
<th></th>
<th>Fc-Fusion</th>
<th>mAbs</th>
<th>Fab (Certolizumab)</th>
<th>Bispecific</th>
</tr>
</thead>
<tbody>
<tr>
<td>Protein</td>
<td>13.2 g/l</td>
<td>24.5 g/l</td>
<td>14.5 g/l</td>
<td>1.04 g/l</td>
</tr>
<tr>
<td>Yield</td>
<td>168 Hours</td>
<td>168 Hours</td>
<td>164 Hours</td>
<td>144 Hours</td>
</tr>
<tr>
<td>Purity</td>
<td>1.89 g/l/day</td>
<td>3.5 g/l/day</td>
<td>2.1 g/l/day</td>
<td>0.17 g/l/day</td>
</tr>
</tbody>
</table>

Proof of Principal for Antigen Classes Routinely Used in Vaccines

<table>
<thead>
<tr>
<th>Antigen Class</th>
<th>Yield</th>
<th>Purity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemagglutinin (HA)</td>
<td>413 mg/l</td>
<td>72 mg/l/day</td>
</tr>
<tr>
<td></td>
<td>137 Hours</td>
<td></td>
</tr>
<tr>
<td>Antigen</td>
<td>1,780 mg/L</td>
<td>350 mg/l/day</td>
</tr>
<tr>
<td></td>
<td>121 Hours</td>
<td></td>
</tr>
<tr>
<td>Virus-Like Particles</td>
<td>2,200 mg/L</td>
<td>500 mg/l/day</td>
</tr>
<tr>
<td></td>
<td>110 Hours</td>
<td></td>
</tr>
</tbody>
</table>
MAbY Binding Assay by Biacore T200

Studying the interaction of mAbs in real time

MAbY for which the ligand was commercially available was produced in CHO (control Mab) and C1 (C1-produced mAb)

The control mAbY and C1-produced MAbY showed virtually indistinguishable binding kinetics.

The binding properties of a pharma’s mAbs to the ligand were compared in a Biacore T200 assay

Similar results were obtained with other mAbs

<table>
<thead>
<tr>
<th>CHO-produced</th>
<th>Multi-cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>ka (1/Ms): 1.033E+5 ± 80</td>
<td>ka (1/Ms): 1.056E+5 ± 63</td>
</tr>
<tr>
<td>kd (1/s): 3.539E-4 ± 6.2E-7</td>
<td>kd (1/s): 4.821E-4 ± 7.3E-7</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>C1-produced</th>
<th>Multi-cycle</th>
</tr>
</thead>
<tbody>
<tr>
<td>ka (1/Ms): 1.069E+5 ± 88</td>
<td>ka (1/Ms): 1.085E+5 ± 230</td>
</tr>
<tr>
<td>kd (1/s): 3.601E-4 ± 8.6E-7</td>
<td>kd (1/s): 5.097E-4 ± 8.4E-7</td>
</tr>
</tbody>
</table>

Capture:

An%-mAb

Analysed:

mAb

Immobilization:

α-Human Fc & α-Mouse Fc
Neutralizing activity of mAb produced in fungus or CHO cells

Hemolytic assay in rabbit RBC with alpha toxin of *Staphylococcus aureus*

The neutralizing activity assay demonstrated great similarity between C1 produced mAb and CHO produced mAb.

Hemoglobin was measured at OD450 in supernatants.
Bispecific Produced in C1 and CHO Have Identical/Similar Activity

- The function of C1-produced bispecific was compared to the CHO-produced control in a bioassay
  - C1-produced purified using only single chromatography step
  - CHO-produced fully purified
- Potency of C1-produced bispecific in the bioassay is comparable to the CHO-produced control
- No negative effects of the C1-derived potential impurities in cellular assays
- The native C1 glycan structure is more mammalian-like than that of yeast
  - Native C1 glycans are mostly high mannose type (Man3-Man9) including low amount of hybrid glycans
  - We have successfully completed initial glycoengineering of C1 cells
  - We now have Four (4) Novel C1 Cell Lines with different glycan patterns
    - (i) Man_{3-9}, (ii) Man_3, (iii) G0 and (iv) G2
Applying C1 Technology in Collaborations and on Our Own Account…
Our Approach to Business Development and to Selection of Internal Programs

We meet our business partners and research collaborators where they are, seeking to leverage our C1 technology at little or no cost to us:

For big pharm companies focused on specific therapeutic agents, we seek funded Proof of Concept (POC) collaborations followed by up front access fees, milestones and royalty arrangements.

For small biotechnology firms, we seek equity, milestones and royalties. We own 7.5% of Alphazyme, 20% of Novovet, 16.1% of BDI Group, and 16.3% of VLP Bio.

1 Upon successful transfer of the C1 technology platform and training we are expected to receive 7.5% equity of Alphazyme.
ZAPI, is a research and development program sponsored by the EU with the goal of developing a platform suitable for the rapid development and production of vaccines and protocols to fast-track registration of developed products to combat epidemic Zoonotic diseases that have the potential to effect the human population.

https://www.imi.europa.eu/projects-results/project-factsheets/zapi

➢ SBV causes congenital malformations and stillbirths in cattle, sheep, goats, and alpaca.

➢ An antigen against Schmallenberg Virus (SBV) that was developed by ZAPI group, was expressed by C1 (next slide).

➢ The C1 expressed SBV antigen that was assembled to Nano-particle expression molecules was tested in animal tests:
  o All immunized mice survived challenge infection without any clinical signs of disease. Protection was conferred even after only one immunization.
  o Cattle were completely protected, the particles conferred sterile immunity (no virus replication after challenge infection) after 2 immunizations
The production volume that will be needed to produce 1 batch of 100K, 1,000K and 10,000K SBV doses with C1 (1.75 g/L)

C1 fermentation is based on Fed-batch technology with glucose feeding and synthetic media.

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<tr>
<th>Doses per batch (20ug/dose)</th>
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<tr>
<td>Total volume (g)</td>
<td>2</td>
<td>20</td>
<td>200</td>
</tr>
<tr>
<td>Productivity (g/L)</td>
<td>1.75</td>
<td>1.75</td>
<td>1.75</td>
</tr>
<tr>
<td>Recovery (%)</td>
<td>75</td>
<td>75</td>
<td>75</td>
</tr>
<tr>
<td>Working volume (%)</td>
<td>80</td>
<td>80</td>
<td>80</td>
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<td>Fermentation volume needed for 1 batch run with C1</td>
<td>2L</td>
<td>20L</td>
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E.Coli and Baculovirus would require between 7,000 L to 20,000 L capacity for 10,000 K dosages vs 200 L using C1.
C1 Expressed ALL seven (7) of the Sanofi therapeutic and vaccine proteins in the feasibility study

- C1 expressed more than half of the seven proteins at or exceeded the production levels initially set by Sanofi.

- We expect a decision by Sanofi sometime in Q2 or Q3, 2020 as to if, and how they may want to proceed.
Dyadic and Serum to Develop and Manufacture Affordable and Accessible Antibody Products and Vaccines Globally

Serum Institute of India

- World’s largest vaccine manufacturer -- > 1.3 billion doses
- Serum supplies vaccines to more than 140 countries
- 65% of the children in the world receive at least one vaccine produced by Serum Institute(1)
- Scope of Research and Commercialization Collaboration:
  - To develop and manufacture 12 antibodies and vaccines using Dyadic C1 Gene Expression Platform
  - Potential for downstream milestones and royalties

“Serum has a proven track record of more than 50 years of developing and delivering affordable vaccines and drugs globally and we are eager to incorporate Dyadic’s industrially proven C1 gene expression platform into our antibody and vaccine development and manufacturing programs. Dyadic’s C1 gene expression platform has the potential to help us deliver on our commitment to bring down the cost of biologics in order to make them more accessible and affordable to patients globally.”

Adar Poonawalla, CEO
Serum Institute of India
Dyadic and The Israel Institute for Biological Research (IIBR) Expand Collaboration to Combat Emerging Diseases

The Israel Institute for Biological Research “IIBR” is a governmental, applied research institute specializing in the fields of biology, medicinal chemistry and environmental sciences.

IIBR will explore the potential of Dyadic’s industrially proven C1 gene expression platform to express gene sequences and targets developed by IIBR into both an rVaccine candidate and monoclonal antibodies (mAbs) that may help combat the outbreak of the COVID-19 virus (Coronavirus).

The research collaboration combines IIBR’s renowned scientific capabilities and cGMP facilities with Dyadic’s patented and proprietary C1 gene expression platform known to shorten the development cycle, lower the manufacturing cost and improve the performance of vaccines and mAbs.

PAST SUCCESS WITH IIBR: In our collaboration with IIBR, a proprietary IIBR Fc-fusion enzyme has been expressed using our C1 technology. This Acetyl Choline Esterase enzyme has previously been shown to provide certain countermeasures against nerve agents such as sarin and VX gas which are toxic and rapidly acting chemical warfare agents. The recombinant IIBR Fc-fusion enzyme, produced in HEK293 cells, has been shown to provide longer lasting protection than the common Acetyl Choline Esterase
Coronavirus Opportunities – C1 Gene Expression Platform

Working together we can “Keep The World Safe” by helping to address the immediate coronavirus outbreak, be better prepared for future infectious diseases, pandemic, and epidemic outbreaks, and leveraging this unfortunate situation to advance biopharmaceutical manufacturing to help speed development, lower the cost and improve the performance of biologic vaccines and drugs such as insulin, seasonal flu and other vaccines and antibodies to make healthcare more accessible and affordable to patients.

C1, has potential to produce larger quantities of lower cost more potent recombinant Vaccines and drugs for Pandemic and Epidemic zoonotic diseases and biologic threats

Coronavirus Opportunities

- Israel Institute for Biological Research (IIBR)
- Zoonotic anticipation and preparedness initiative (ZAPI)
- UfoVax / (Scripps Spin Out Company)
- Cr2o, Erasmus, Utrecht, TiHo Hannover (Select ZAPI Institutes (1))
- Vaccine Clinical Materials Program, Fredrick National Laboratory
- Other Ongoing Discussions

(1) ‘Coronavirus, Global Expert Landscape Analysis 2020’ https://drive.google.com/file/d/1LD_6F5QC3JVS1xKWB38auGuhg2MUI7PA/view
Albert Osterhaus (ranked #3), Bart Haagmans (#16), Berend Jan Bosch (#18).
Coronavirus spike receptor binding domain: key target for potent neutralizing Abs

- Receptor Binding Domain (RBD)

- ACE2 receptor

Antigen minimization

Receptor binding domain:
- Single folded polypeptide chain
- All potent neutr. Ab target the RBD
- Ag minimization -> focused immune response
UfoVax / (Scripps Research Institute)

Ufovax, Inc. and Its 1c-SApNP® Technology Towards An Effective 2019-nCoV Vaccine

• Single-component self-assembling protein nanoparticle (1c-SApNP®), streamlines vaccine development that targets:
  The picture on the left is one of the first electronic microscopy (EM) images taken for several 2019-nCoV vaccine candidates.
  Our immune system is expected to recognize this vaccine in a virus like particle form more effectively and generate antibodies that can neutralize (deactivate) the coronavirus.
  Animal studies needed to be finalized, sequence synthesized and inserted in a host cell, such as C1 for mass production

• Animal models for assessing vaccine-induced broadly neutralizing response
• Wildtype/humanized mouse models • Rabbit models • Various nonhuman primate (NHP) models

• C1 expression of two 1c-SApNP HIV vaccines
The Rapidly Growing C1 Glycoform Cell Lines / Dialing up & Down Immunogenicity

Achievements so far: The Glycoengineering of C1 has generated good results to date

Four C1 Strains (Glyco structures on C1 native proteins)

Native C1 Man$_{3,9}$ Strain

Man$_{3,9}$ with hybrid glycoforms

C1 M3 Strain

99% M3

C1 G0 Strain

95% G0

C1 G2 Strain

76% G2
The production volume that will be needed to produce 1 batch of 100K, 1,000K and 10,000K SBV doses with C1 (1.75 g/L)

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E.Coli and Baculovirus would require between 7,000 L to 20,000 L capacity for 10,000 K dosages vs 200 L using C1.
Sanofi Vaccine Trial and Model Vaccine

Murine Immunogenicity Study of HA/NC Produced by C1 vs. baculovirus

Recombinant Hemagglutinin (HA) produced in C1 is well tolerated in mice
- No weight loss
- No negative clinical signs

HA/New Caledonia from C1 has excellent immunogenic properties

Superior response than control HA/New Caledonia produced in baculovirus

C1 can produce high amounts of HA (~1 g/L) and other antigens in 3-7 days by using low cost fermentation

Large market opportunity: 146M influenza doses/year

Each 0.5 mL dose typically contains: 15 µg of HA for each strain

Thus, three 1000L C1 fermentation runs theoretically can supply the annual global HA demand of ~2,175 g

<table>
<thead>
<tr>
<th>Expression System</th>
<th>Dose of rHA 1 u/g</th>
<th>Dose of rHA 3.3 u/g</th>
<th>Dose of rHA 10 u/g</th>
<th>Dose of rHA 30 u/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>50% (4/8)</td>
<td>57% (4/7)</td>
<td>100% (8/8)</td>
<td>100% (8/8)</td>
</tr>
<tr>
<td>Baculovirus</td>
<td>62% (5/8)</td>
<td>12% (1/8)</td>
<td>50% (4/8)</td>
<td>75% (6/8)</td>
</tr>
</tbody>
</table>

Seasonal Flu – C1 Gene Expression Platform

C1, has potential to produce larger quantities of lower cost more potent recombinant seasonal flu vaccines

Sanofi Pasteur Conclusions (1):

1. The full length recombinant HA from the A/H1N1/New Caledonia/20/99 strain produced in Myceliophthora thermophila (C1 fungi) did not induce any clinical signs in mice ✓

2. The full length recombinant HA from the A/H1N1/New Caledonia/20/99 strain produced in Myceliophthora thermophila (Dyadic) is at least as immunogenic as the baculovirus-rHA (Protein Sciences) in mice ✓

<table>
<thead>
<tr>
<th>Expression System</th>
<th>Dose of rHA 1 u/g</th>
<th>Dose of rHA 3.3 u/g</th>
<th>Dose of rHA 10 u/g</th>
<th>Dose of rHA 30 u/g</th>
</tr>
</thead>
<tbody>
<tr>
<td>C1</td>
<td>50% (4/8)</td>
<td>57% (4/7)</td>
<td>100% (8/8)</td>
<td>100% (8/8)</td>
</tr>
<tr>
<td>Baculovirus</td>
<td>62% (5/8)</td>
<td>12% (1/8)</td>
<td>50% (4/8)</td>
<td>75% (6/8)</td>
</tr>
</tbody>
</table>

University of Oslo consortium and Dyadic have agreed to enter into a feasibility study whereby University of Oslo can evaluate the C1 technology

The purpose of the feasibility study is to demonstrate the potential viability of Dyadic’s C1 technology to express APC-targeted Influenza virus antigen proteins, provided by Oslo University, that may lead to further collaborations between the parties for the expression and production of vaccine proteins with the C1 production platform.

The specific goals of the project are:

a. To evaluate the expression of the following University of Oslo proteins in the C1 fungal host system of Dyadic.

b. To conduct protein analysis by Oslo University to evaluate the quality of each of the expressed proteins.
Dyadic’s Certolizumab (Cimzia) Biosimilar Program

Certolizumab is a pegylated Fab’ antibody fragment targeting TNFα; indicated for various rheumatic diseases

Cimzia 2018 sales of € 1.44 billion for UCB

C1 produces certolizumab in inexpensive single use bioreactors or in stainless steel bioreactors (SSB) with equivalent yields

SSB Yield of 14.5 g/l in 7 days fermentation

Results between batches are consistent, showing the robustness of the technology

Certolizumab production in SUB (g/L)

<table>
<thead>
<tr>
<th>Conditions</th>
<th>Single Use Bioreactor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Initial medium: 25L</td>
<td></td>
</tr>
<tr>
<td>Final broth: 32kg</td>
<td></td>
</tr>
<tr>
<td>d02 controlled by air flow and Pure oxygen addition.</td>
<td></td>
</tr>
<tr>
<td>Titer / Time</td>
<td>9.2 g/L at 112 hrs</td>
</tr>
<tr>
<td>Productivity</td>
<td>2.0 g/L/day</td>
</tr>
</tbody>
</table>

Equipment: 50L XDR-50MO

Single Use GE bioreactor

Product protein: Certolizumab
**Roadmap for Biosimilar Certolizumab Development**

**USP&DSP development**
- In Bench scale C1 using protein L

**Year 1**
- Cell line development

**Year 2**
- CMC development

**Year 3 – Year 6**
- Biological activity comparison
- Structural comparison
- Non-clinical comparison
- Clinical comparison

**Analytics to compare the structural & physicochemical characteristics of product vs. commercial reference**
- In vitro assays to compare product mechanisms of action.
  - Primary: TNFα neutralization by binding and inhibition of cell signaling for proliferation
  - Secondary: activation of immune responses as CDC, ADCC....

**CMC development and batches production (GMP for clinical assays)**
- Optimization of process & product quality attributes profile, cell line characterization & stability, formulation & product stability testing.

**DYADIC INFORMATION**

- 1 year Phase I trial to determine PK equivalence (mainly safety) in AS patients (250)
- 2 year Phase I pilot study for RA patients (19)
- 1 year Phase III trial to mainly determine therapeutic equivalence in RA patients (606)

**Generation of producing strain**
- In 30L bioreactor
- 14.5 g/l, (2.4 g/l/day) production rate
- Based on EMA assessment report for approval of an Infliximab (anti-TNFα) biosimilar (2013)
- (1) O-glycosylation has recently been identified in Certolizumab, it will need to be reduced or removed

**In vitro PD studies to compare neutralization. activity, CDC, ADCC and apoptotic effects and cross-reaction with human tissues**
- In vivo PK studies to detect products in animal serum & to measure anti-products Ab concentration
- In vivo toxicity & toxic kinetics assays
Dyadic’s Nivolumab (Opdivo®) Biosimilar Program

The immunotherapy drug Opdivo (nivolumab), manufactured by Bristol Myers Squibb, is indicated for metastatic cancers, including melanoma and lung cancer.

Opdivo is priced at $12,500 a month, or about $150,000 for a year of treatment, and is projected to have $8.0 B peak sales.

Our goal is to create a glycoengineered C1 cell line that will express nivolumab (mAb) with a glycan structure similar to nivolumab produced from CHO cells.

We have created a glycoengineered C1 cell line with ~95% G0 level.

1 Trefis team Analyst Opdivo Estimate for 2023
Potential Use of C1 to Produce Associated Virus (AAV) Vectors


- As new gene therapies are approved by the FDA, there’s a backlog in the production of therapeutic viruses
- Manufacturing disabled viruses (typically a disabled adenovirus or lentivirus) is costly and onerous

Recombinant Adeno-Associated Virus (AAV) Vectors
- A widely used vehicle for delivering gene therapy to humans
- Used in nearly 50% of the 483 currently ongoing gene therapy trials, and use likely to persist
  ✓ Wild-type AAV does not cause human disease
  ✓ AAV can transduce non-dividing as well as dividing cells, unlike other viral vectors.
  ✓ Robust transgene expression has been observed in several Phase I and II trials.
  ✓ Distinct AAV vector serotypes target different tissues, organs, and cells, thus expanding potential therapeutic utility
  ✓ Efforts in large markets (Alzheimer’s Disease, Parkinsons, RA) necessitate better ways of manufacturing AAV

Global Opportunity Analysis and Industry Forecast, 2017-2023, estimates a large market opportunity:

"the global gene therapy market accounted for $584 million in 2016, and is estimated to reach $4,402 million by 2023, registering a CAGR of 33.3% from 2017 to 2023"
Applying C1 to Produce Metabolites

**Primary metabolite**
- Dyadic collaborated with a third party to develop C1 strain for a high yield, low cost primary metabolite product
- Dyadic is using precise genetic manipulation that is based on metabolic modeling and synthetic biology
- Funded by the third party
  - Phase 1 milestone achieved
  - Phase 2 terms, including strain optimization and manufacturing agreement, under discussion
  - Dyadic has option to pursue program independently

**Secondary metabolite**
- Project initiated by Dyadic
- Centered on a class of high-value secondary metabolites used in pharmaceutical, cosmetic, and wellness applications

Our *in silico* metabolic model supports precise engineering of C1 for optimal primary and secondary metabolites production:
Dyadic Investment Thesis

Proprietary Technology - C1 Fungal Gene Expression Platform - Broad Applications

- Recent Nasdaq Listing; Compelling Valuation
  - April 17, 2019
  - Up-listed on Nasdaq Capital Markets

- Funded On-going R&D Collaborations with Top Tier Pharm

- Experienced Board Members and Management Team

- Strong Balance Sheet
  - US$37.2M cash & equivalents\(^1\)
  - No Debt or Warrants

- Proven Technology for Industrial Use
  - Success in Industrial Use
  - Over Two Decades Of Biotechnology Experience
  - Sold Industrial Biotech Unit to DuPont for $75M in 2015

\(^1\) As of September 30, 2019, incl. accrued Interest
THANK YOU!