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DYADIC INTERNATIONAL: WORKING TO CHANGE THE GAME IN BIOPHARMA MANUFACTURING

DYADIC® IT

Mark Emalfarb, Founder, President and Chief Executive Officer, and **Matthew Jones,** Chief Commercial Officer at **Dyadic International, Inc.**

Key learnings:

- Dyadic International, Inc. has developed a fungus-based gene expression platform, C1, which it believes could provide significant advantages over existing technologies, such as CHO cells.
- Following an established history in industrial applications, the company is now exclusively working to leverage its platform to deliver scale and cost efficiencies to the pharmaceutical sector.
- Mark Emalfarb (pictured, left), Founder, President and Chief Executive Officer, and Matthew Jones (pictured, right), Chief Commercial Officer, spoke to LSX about the potential benefits and healthcare applications of the C1 platform, and explained why he believes new manufacturing approaches have a key role to play in helping the healthcare industry address the challenges it is facing.

Since 2016, Dyadic International, Inc.'s strategic focus has been on improving the development and production of protein-based biologics and vaccines through its gene expression platform, C1. The company, which is listed on the American exchange OTCQX and whose footprint spans the US and Europe, has a long-standing and somewhat unusual history.

Founded by Mark Emalfarb in 1979 to pioneer the use of pumice stones to stonewash blue jeans, the company transitioned to enzyme use for this process in the 1980s as the industry advanced. In the early 1990s, Dyadic began working with a filamentous fungal strain known as C1. As a result of two serendipitous mutations over the course of C1's development, not only did the morphology change allowing for greater productivity and scale, but it also enabled increased protein purity at a higher yield and lower cost. C1 has since been utilised in a number of commercial products and large-scale industrial applications, including by international corporations such as BASF, DuPont, and Shell. "It's an industrial workhorse. It's very productive, robust and versatile," says Emalfarb. "For years we sold enzymes into 35 countries for animal feed, biofuels, food, and textiles."

On 31 December 2015, DuPont acquired Dyadic's industrial technology business for $75 million in cash. Under the terms of the agreement, Dyadic retains co-exclusive rights to C1 technology in animal and human pharmaceutical applications and it has the exclusive rights to sub-license the technology in these areas. The company has since been dedicated to leveraging its industrially-proven technology to enhance biopharmaceutical manufacturing and to offer an alternative to expression platforms such as Chinese hamster ovary (CHO) cells. Its focus lies on further developing C1 technology for vaccines, antibodies, biosimilars, biobetters, and other therapeutic proteins.

"It's taking the power of industrial biotech and bringing it into the pharmaceutical industry," says Emalfarb. "That power is the ability of a cell to produce a lot more, a lot quicker, with lower-cost nutrients, and without the need to perform viral inactivation."

Disrupting established processes to address industry challenges

Dyadic sees its technology as a potential disruptor to the use of established gene expression platforms, delivering cost and efficiency savings, including the possibility of reducing capital and operational expenditure. "A CHO cell takes 20 hours to double. C1 takes

two hours. By a factor of 10 you can go faster, and that helps you in discovery, in development, as well as production in the tank. Today, [C1 production takes] four to seven days, and CHO cells are typically 14 days," explains Emalfarb. "For the time you're in the fermenter, every day is a cost, but it is half-to-one-third [with C1] than with a CHO cell. So, in half the time you can make two-to-10 times more, and the nutrients you use to feed it are one tenth-to-one 25th the cost. It's a multiple advantage."

As biopharma companies and healthcare systems face increasing pressures, Emalfarb believes new approaches are required to deliver long-term solutions. He says: "How we view it is that [pharmaceutical companies] have been using an inefficient cell line for over 30 years. They've pushed it, improved it, and made it better, but you can only push it so far." Indeed, a survey conducted by BioPharma-Reporter.com in September 2017, *State of the global biomanufacturing and bioprocessing industry 2017*, found that 45% of respondents feel that the industry is too reliant on CHO cell lines, and 32% of respondents are unsure.

New gene expression systems, such as C1, could potentially play a role in addressing some of the development and manufacturing challenges companies come up against, which could in turn assist in bringing more drugs to patients at a faster and more affordable rate, notes Emalfarb. He says: "Making healthcare accessible and affordable is an inalienable right of human beings, and I think we're failing. And the reason why we're failing in my opinion, to a great degree, is a lot of bottlenecks in the system."

Dyadic aims to deliver the scale and technology to improve the manufacturing process in order to lower the cost of biologic drugs and vaccines and facilitate the development of new treatments. "It's not just about low-cost production, it's about genes that are stuck in research programmes, cures to diseases sitting in cells that aren't being produced at sufficient levels to allow research to [continue] on an affordable basis," points out Emalfarb. This goal is summed up by the company's mantra: making the unmakeable.

Building on biologics and vaccines collaborations

Dyadic has established a number of industry partnerships to explore the potential of its technology across different healthcare applications. In September 2018, it announced a proof-of-concept research collaboration with Sanofi-Aventis Deutschland GmbH, part of the Sanofi group, to examine the potential of the C1 platform to express multiple genes for vaccine and drug applications. The research is due to conclude in 2H19.

Matthew Jones, Chief Commercial Officer, notes that Dyadic's other disclosed collaborations include a proof-of-concept research programme with Mitsubishi Tanabe Pharma Corp., which focuses on the production of two therapeutic proteins using C1 technology, as well as a research and development collaboration with the Israel Institute for Biological Research (IIBR). The activities conducted through the collaboration with IIBR centre around the evaluation of C1 for the development and manufacture of recombinant vaccines and neutralising agents, including targeted antigens and monoclonal antibodies. "That [collaboration] is enabling the country of Israel to potentially better defend its population, to be able to deal with emerging diseases, pandemics, epidemics, and threats," says Emalfarb.

The company is also participating in the Zoonoses Anticipation and Preparedness Initiative (ZAPI). This project is funded by the Innovative Medicines Initiative (IMI), a large-scale public-private partnership between the European Union and the European Federation

of Pharmaceutical Industries and Associations (EFPIA). As part of this research initiative, Dyadic Nederland B.V. is utilising the C1 technology platform to express neutralising agents and vaccines.

Dyadic is looking to collaborate further with governmental agencies and industry to harness the potential benefits of its technology in the development and production of vaccines, such as the flu vaccine. Jones says: "We're approaching to work with the US government and other institutions across the globe to help better defend populations in each of those countries, and to help them make quicker, better, faster vaccines that can get to people sooner."

In addition to working with industry partners, Dyadic can draw on a wealth of in-house experience; the company has been developing C1 technology for more than 20 years. Its board and leadership team also have expertise across senior research, development, manufacturing, and strategic leadership roles. The newest addition to its board of directors, Dr Barry Buckland, spent 29 years at Merck, where he most recently held the position of Vice President Bioprocess R&D, Merck Research Laboratories.

Leveraging partnerships for continued progress

As it beds deeper into the biopharma industry, Dyadic continues to work to refine its platform. For example, it has now achieved a production rate of 9g/l in 90 hours for monoclonal antibodies or 2.4g/l per day, and 1.9g/l per day for Fab antibody fragments.

Optimisation remains a key objective for the company over the next 12-18 months. "We're working on speeding up development and discovery of proteins using a cell line," says Emalfarb.

"And we're looking for partners to help us move that along. We're looking to find more people who have gene stocks sitting on a shelf for cures for diseases who need help to make sufficient quantities of proteins to move the research forward."

Dyadic intends to establish new partnerships to exploit the full potential of its gene expression platform, and progress towards its ultimate aim of supporting more affordable and accessible treatments for patients. "We need to get [C1] technology into the hands of research scientists across the globe at early stages as an alternative, additional expression [platform] to E. coli and CHO cells," explains Emalfarb. "The more people that work with it, the faster it will be adopted, developed to higher and higher levels, and bring medicine to people more affordably. That's really the goal, and we're making great progress along that path."

Note: *You can learn more about Dyadic and its gene expression system at the Inv€$tival Showcase in London on 13 November 2018, where Mark Emalfarb and Matthew Jones will be in attendance to present the latest developments at the company.*

Written by Louise Fordham, Editor at LSX, formerly Biotech and Money. This article was first published in October 2018 on www.lsxleaders.com.

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Dyadic International, Inc.

Dyadic International, Inc. is a global biotechnology company focused on improving and applying its proprietary C1 gene expression platform, based on a patented and proprietary genetically modified strain of the fungus Myceliophthora thermophila, to address opportunities in the human and animal health markets. C1 is a potentially game-changing biopharmaceutical gene expression platform that may help bring biologic drugs to market faster than existing expression platforms, such as Chinese hamster ovary (CHO) cells, E. coli and others, in greater volumes, at lower cost and with new properties that can improve access and cost to patients and the healthcare system. Dyadic is seeking partnerships to sub-license or partner its C1 platform technology in the vaccine, antibody and biosimilar industries.

For further information, please visit: www.dyadic.com