May 17, 2022

Oragenics Issues Letter to Shareholders

TAMPA, Fla.--(BUSINESS WIRE)-- **Oragenics, Inc. (NYSE American: OGEN) ("Oragenics" or the "Company")** today issued the following letter to shareholders from its Executive Chairman, Frederick W. Telling, Ph.D.:

To My Fellow Shareholders,

I am pleased to share with you an update on Oragenics' vaccine development strategy, as well as to discuss how our intranasal SARS-CoV-2 vaccine candidate holds potential to play an important role in addressing the pandemic and endemic phases of COVID-19 and how it shapes our long-term corporate goals. I thank you for your continued support of Oragenics and our vision, and am delighted to report on our recent progress.

In previous letters I affirmed the strategic direction Oragenics is taking and discussed our commitment to the speedy yet prudent execution of our development work. I also explained how securing additional complementary partner agreements fundamentally differentiates our program by providing the technology to improve the strength, versatility and manufacturing efficiency of our intranasal COVID-19 vaccine candidate, NT-CoV2-1. Through this letter I aim to provide clarity on the opportunity, rationale and pathway toward human clinical testing.

We believe that given the scope of the pandemic along with additional vaccines projected to become available, there will be considerable demand for our highly differentiated NT-CoV2-1 vaccine once development is successfully completed. We intend to combine the research, intellectual property protection and biological materials covered by our NIAID license with our existing clinical research and manufacturing capabilities to respond to this ongoing, global public health crisis. With our research collaborations and recent extensions that enable us to pursue future variants, we believe our NT-CoV2-1 vaccine holds the promise of playing an important role in addressing this crisis.

NT-CoV2-1, a Novel Approach to Vaccine Development

Oragenics' NT-CoV2-1 program leverages coronavirus spike protein research licensed from the National Institutes of Health (NIH) and a Chinese Hamster Ovary (CHO) cell line expression system licensed from the National Research Council of Canada (NRC). We believe it provides an agile production platform that supports faster development of spike protein antigens, or immune system response stimulants, to address new SARS-CoV-2 variants as they emerge. Importantly, our recently extended platform could allow for the production of cell lines within six to eight weeks of spike gene sequence availability, compared with six to nine months for traditional production of such cell lines, thereby expediting evaluation of future intranasal vaccine candidates in preclinical and clinical

studies. The spike protein is formulated with a proteosome-based mucosal adjuvant (BDX301) to enable intranasal immunization.

Market Positioning

The overall disease burden from COVID-19 has continued to increase in the U.S. despite 91% of those age 65 or older being fully vaccinated and 71% of those age 5 or older. Current vaccines have reduced the rates of hospitalization and death due to COVID-19 in vaccinated individuals, but the transmission levels even in vaccinated individuals has allowed SARS-CoV-2 variants to continue to circulate. We believe an intranasally-administered vaccine against COVID-19 has the potential to reduce transmission more effectively than those delivered intramuscularly because the intranasal route is expected to induce mucosal immunity in the nose and throat, which are the early entry points for the SARS-CoV-2 virus.

Our primary focus remains on developing our intranasal administered vaccine, NT-CoV2-1, as a single-dose booster since the market opportunity for COVID-19 vaccines will likely evolve as more of the global population receives their primary vaccine doses this year and next.

Among other factors, the market for booster doses will be driven by the need for updated vaccines to provide protection against future virus variants, as well as vaccines for unvaccinated infants and children. Oragenics is positioning NT-CoV2-1 to compete in this later phase of the COVID-19 pandemic.

Preclinical Development Overview & Next Steps

We began preclinical studies in June 2021 through our collaboration and material transfer agreement with the NRC. We initiated an immunogenicity study in mice to evaluate several adjuvant candidates. Last August, we announced the successful completion of these mouse immunogenicity studies, which support further development using either the intramuscular or the intranasal route of administration. We initiated a hamster challenge study in September 2021 to assess inhibition of viral replication using adjuvants specific for intramuscular and intranasal administration.

In December of 2021, we announced that the vaccines delivered by intranasal and intramuscular routes in hamsters, both generated robust immune responses and reduced SARS-CoV-2 viral loads to undetectable levels in the nasal passages and lungs five days following a viral challenge. By contrast, hamsters in the control groups that had received saline or adjuvants alone had no detectable immune response along with substantial viral loads.

GLP Toxicology Study

In March of 2022, following a positive assessment of a rabbit-based pilot study, we initiated a Good Laboratory Practice (GLP) toxicology study to evaluate the safety profile and immunogenicity of NT-CoV2-1 in rabbits. This important preclinical study is designed to provide data required to advance our intranasal vaccine candidate into human clinical studies. Although the study remains underway, based on our previous preclinical results we are encouraged that this study may further support our intranasal development path.

Regulatory Strategy

The completion of the rabbit toxicology study is the final element of our preclinical development work, prior to initiating a Phase 1 clinical study in North America with NT-CoV2-1, the protocol for which is currently under development.

In parallel with our pursuit of an IND for a US-based Phase 1 study, Oragenics is exploring regulatory approval for an equivalent safety and immunogenicity study with Health Canada through the submission of a Clinical Trial Application (CTA). Given Health Canada's experience with related adjuvants to that used in NT-CoV2-1 and the growing urgency for nasal vaccine solutions, we believe this alternate regulatory path remains a viable route for maintaining our development timelines.

Benefits of Intranasal Vaccine Delivery

As discussed, we remain focused on our intranasal candidate, NT-CoV2-1, as we see its innate benefits as key points of differentiation in combatting the COVID-19 pandemic and increasing access to vaccines globally. Our vaccine candidate has many potential competitive features and benefits, including:

- **Targeting Mucosal Immunity –** Conventional injectable vaccines are poor inducers of mucosal immunity, whereas intranasal immunization can induce strong mucosal immunity by enhancing the immune response at the entry sites of mucosal pathogens. When the SARS-CoV-2 virus enters the nasal cavity, the respiratory epithelial layer is the first barrier against viral infection. The intranasal route of vaccination provides two additional layers of protection over intramuscular shots because (i) it produces immunoglobulin A and resident memory B and T cells in the respiratory mucosa that are an effective barrier to infection at those sites, and (ii) cross-reactive resident memory B and T cells can respond earlier than other immune cells should a viral variant start an infection.

- **Needle-Free Administration –** As an obvious benefit, intranasal administration means needle-free delivery, resulting in meaningful differentiation for children and needle-phobic populations, improved compliance and the potential for self-administration.

- **Storage & Transport –** The currently available mRNA-based vaccines have been delivered globally via stringent storage and transport requirements that strain distribution logistics under the best of circumstances. A key benefit of our NT-CoV2-1 candidate is a significantly reduced handling burden, allowing transport at a more manageable refrigeration temperature (5°C) that improves access globally including remote and under-vaccinated geographies.

- **Durability –** Broad initial success with mRNA vaccines has significantly diminished COVID-19's impact and death, but the trade-off has been fleeting efficacy. By benefitting from the immunological properties of the hybrid NIH/NRC construct, NT-CoV2-1 is potentially much more durable and long-lasting than currently available mRNA-based therapies.

Our Balance Sheet

We expect to use current cash resources to advance the development of NT-CoV2-1 through IND-enabling studies, including immunogenicity, viral challenge studies, toxicology studies and the Phase 1 trial. Subsequent clinical development will be contingent upon the receipt of additional funding, including non-dilutive government grant funding we continue to pursue, or securing a partnering or licensing transaction.

2020 Annual Meeting

As a final topic, I would like to thank the shareholders who voted at our reconvened 2020 Annual Meeting, which was ultimately successfully held in February 2022. We are pleased that a majority of shareholders signaled support for amendments including (i) an increase of 50,000,000 authorized shares of common stock going from 200,000,000 to 250,000,000 shares, and (ii) a reduced quorum requirement from a majority of shares entitled to vote to one-third of shares entitled to vote in order to constitute a meeting of shareholders. The latter amendment significantly reduces the likelihood of having to reconvene an annual meeting simply because a quorum could not be met, as we experienced this past year.

Looking Ahead

In closing, I am very excited about the future of Oragenics to become a leader in intranasal vaccine technology and am optimistic about our candidate's market positioning. On behalf of the Oragenics Board of Directors, I thank you for your continued support and look forward to keeping you apprised of our ongoing progress.

Sincerely,

Frederick W. Telling
Executive Chairman

May 17, 2022

About Oragenics, Inc.

Oragenics, Inc. is a development-stage company dedicated to fighting infectious diseases including coronaviruses and multidrug-resistant organisms. Its lead product is NT-CoV2-1, an intranasal vaccine candidate to prevent COVID-19 and variants of the SARS-CoV-2 virus. The NT-CoV2-1 program leverages coronavirus spike protein research licensed from the NIH and the NRC with a focus on reducing viral transmission and offering a more patient-friendly intranasal administration. Its lantibiotics program features a novel class of antibiotics against bacteria that have developed resistance to commercial antibiotics. For more information about Oragenics, please visit www.oragenics.com.

Forward-Looking Statements

This communication contains "forward-looking statements" within the meaning of the safe harbor provisions of the U.S. Private Securities Litigation Reform Act of 1995. These forward-looking statements are based on management's beliefs and assumptions and information currently available. The words "believe," "expect," "anticipate," "intend," "estimate," "project" and similar expressions that do not relate solely to historical matters identify forward-looking statements. Investors should be cautious in relying on forward-looking statements because they are subject to a variety of risks, uncertainties, and other

factors that could cause actual results to differ materially from those expressed in any such forward-looking statements. These factors include, but are not limited to, the following: the Company's ability to advance the development of its vaccine candidate and lantibiotics candidate under the timelines and in accord with the milestones it projects; the Company's ability to obtain funding, non-dilutive or otherwise, for the development of the vaccine and lantibiotic product candidates, whether through its own cash on hand, or another alternative source; the regulatory application process, research and development stages, and future clinical data and analysis relating to vaccines and lantibiotics, including any meetings, decisions by regulatory authorities, such as the FDA and investigational review boards, whether favorable or unfavorable; the potential application of our vaccine candidate to variants and other coronaviruses; the Company's ability to obtain, maintain and enforce necessary patent and other intellectual property protection; the nature of competition and development relating to COVID-19 immunization and therapeutic treatments and demand for vaccines and antibiotics; the Company's expectations as to administration, manufacturing, storage and distribution; other potential adverse impacts due to the global COVID-19 pandemic, such as delays in regulatory review, interruptions to manufacturers and supply chains, adverse impacts on healthcare systems and disruption of the global economy; and general economic and market conditions and risks, as well as other uncertainties described in our filings with the U.S. Securities and Exchange Commission. All information set forth in this press release is as of the date hereof. You should consider these factors in evaluating the forward-looking statements included in this press release and not place undue reliance on such statements. We do not assume any obligation to publicly provide revisions or updates to any forward-looking statements, whether as a result of new information, future developments or otherwise, should circumstances change, except as otherwise required by law.

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