September 30, 2022

Oragenics Issues Letter to Shareholders

TAMPA, Fla.--(BUSINESS WIRE)-- **Oragenics, Inc. (NYSE American: OGEN) ("Oragenics" or the "Company"),** a biotech company dedicated to fighting infectious diseases including coronaviruses, today issued the following letter to shareholders from its President and Chief Executive Officer, Kim Murphy.

To My Fellow Shareholders,

As COVID-19 continues to impact the world's population – albeit with far less dire consequences due to the availability of vaccines, therapeutics and better in-hospital care of those with severe disease – a sense of normalcy has returned to daily life. Nonetheless, the persistence of the SARS-CoV-2 virus and its more contagious variants continue to present major global challenges and widespread death. Yet we have become much smarter in our battle against the virus, innovating more durable protection and better controlling transmission.

Perhaps most importantly, we have learned that the best protection against infection with SARS-CoV-2 is achieved by targeting the site of virus transmission, the upper respiratory tract and mouth, which is the focus of Oragenics' ongoing research and development.

We remain confident in our strategic direction and specifically in our plans to advance NT-CoV2-1, our lead intranasal vaccine candidate, into human clinical trials in the first half of 2023. In this letter, I'd like to provide an overview of why I see NT-CoV2-1 as an important component in overcoming this global challenge, and review the current status of our work and next steps.

Benefits & Mechanism of Intranasal Vaccines

As most of you know, in late June I took over the day-to-day leadership of Oragenics from Fred Telling, and we are fortunate that Fred remains a Director of our company. Although I'm new to the CEO role, I'm not new to Oragenics as I have served on the Company's Board of Directors since 2020.

Bringing to my new role more than 25 years of experience in vaccine development, I'm so very proud of the preclinical work the Oragenics team has conducted so far. Collectively we have evaluated various adjuvants and determined that BDX301 provides the optimal path forward by targeting the mucosal immunity that protects against initial infection. Although our preclinical results support development in either the intramuscular or the intranasal route of administration, we believe intranasal delivery holds multiple relative and absolute benefits and, as such, this is the route we are taking which also aligns with industrywide trends in vaccine development.

More specifically, the benefits associated with the intranasal delivery of NT-CoV2-1 include:

- Meaningful differentiation for children and needle-phobic adult populations
- Potential for single-dose efficacy along with enhanced durability
- Significantly easier storage and transport requirements
- The targeting of mucosal immunity

With regard to 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 body's first barrier against viral infection.

In fact, the intranasal route of vaccination provides two additional layers of protection over intramuscular shots because 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. Additionally, cross-reactive resident memory B and T cells can respond earlier than other immune cells should a viral variant start an infection, providing needed durability against evolving variants.

Further Advantages to Our Vaccine Development Approach

Oragenics' NT-CoV2-1 program leverages coronavirus spike protein research that we licensed from the National Institutes of Health (NIH) and a Chinese hamster ovary cell line expression system licensed from the National Research Council of Canada (NRC).

Our program holds potential for faster development of spike protein antigens, or immune system response stimulants, to address new SARS-CoV-2 variants as they emerge. In addition, our platform may allow for the production of cell lines within six to eight weeks after receiving spike gene sequence information, which is far faster than the six to nine months typically required for traditional production of such cell lines.

Favorable Preclinical Profile

This past June we announced the publication of an article co-authored by Oragenics and our collaborators at Inspirevax and the NRC's Human Health Therapeutics Research Centre in *Scientific Reports*, a Nature journal.

The article reported that the intranasal formulation induced robust antigen-specific IgG and IgA titers in the blood and lungs of mice and was highly efficacious in a hamster challenge model, reducing the viral load below the limit of detection. In both mice and hamsters, the antibodies had strong neutralizing activity, preventing the cellular binding of the viral spike protein based on the ancestral SARS-CoV-2 reference strain and certain variants of concern.

These encouraging conclusions enabled us to initiate the currently ongoing toxicology study, which is focused exclusively on the intranasal route of administration.

Status of Our Toxicology Study

The pivotal preclinical Good Laboratory Practice (GLP) toxicology study is evaluating the safety and immunogenicity of NT-CoV2-1 in rabbits, and we expect it to conclude by the end

of this year. In late August we announced preliminary results that continued to demonstrate a safety profile and immune responses that we believe will support regulatory filings to progress to a Phase 1 clinical study, which is a very encouraging checkpoint as we approach the conclusion of the study.

The objectives of this study are to evaluate the potential toxicity of NT-CoV2-1 following repeated intranasal administration at the maximum dose anticipated to be used in human trials, and to confirm the immunogenicity of the vaccine. The only remaining portion of the toxicology report is completion of the ongoing histopathology evaluation, after which Oragenics will package the results into a regulatory application for approval to begin clinical trials.

Regulatory Next Steps

Given Health Canada's experience with the proteasome-based mucosal adjuvant BDX301 and the growing urgency for intranasal vaccines, our optimal path forward is to submit a Clinical Trial Application (CTA) with Health Canada following the completion of the GLP toxicology study. We currently expect to make that submission by early 2023, once the full histopathology report is in hand.

Oragenics is working to expedite the path to market for NT-CoV2-1 and we have optionality with a dual path in both Canada and the U.S. for the necessary Investigational New Drug (IND)-enabling work. Following CTA submission and approval, Oragenics will commence clinical studies in Canada while evaluating the potential for launching parallel studies in the U.S. We currently envision the start of clinical studies in Canada in the first half of next year.

Looking Forward

Our focus remains on developing NT-CoV2-1 as a single-dose booster in the pandemic and endemic phases of the COVID-19 health crisis, and this focus is informed by the evolving market opportunity for COVID-19 vaccines. The market for booster doses is where we expect to position NT-CoV2-1 to compete, and that market will be driven by the need for updated vaccines to provide protection against future variants of the SARS-CoV-2 virus, as well as by the need to vaccinate infants and children.

On behalf of the Oragenics team, as well as our Board of Directors, I want to thank our stockholders for their continued support and I look forward to keeping you updated on our progress as we advance toward a durable solution to the COVID-19 pandemic.

Sincerely,

Kim Murphy
President and Chief Executive Officer

September 30, 2022

About Oragenics

Oragenics, Inc. is a development-stage company dedicated to fighting infectious diseases, including those caused by 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 National Institutes of Health (NIH) and the National Research Council of Canada (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 the outcome of preclinical studies, nasal administration, transmission, 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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