Oyster Point Pharma Announces Preclinical Data Highlighting Potent Activity of OC-01 (varenicline) and OC-02 (simpinicline) Against SARS-CoV-2 Virus and Variants

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- ***Administration of OC-01 (varenicline) nasal spray to non-human primates was observed to inhibit viral replication in the nose within 24 hours of infectious SARS-CoV-2 challenge with absence of subgenomic RNA at Day 3 and Day 5 post-challenge***
- ***Varenicline inhibits cellular entry and replication of SARS-CoV-2 and its alpha and beta variants in multiple human cell types***
- ***Simpinicline inhibits cellular entry and replication of SARS-CoV-2 alpha variant in Calu-3 human cells with additional variants under investigation***
- ***Oyster Point Pharma collaborates with the Trudeau Institute for in vitro testing of varenicline, the active ingredient in OC-01 nasal spray and simpinicline, the active ingredient in OC-02 nasal spray***
- ***Oyster Point Pharma plans to present data at the upcoming Analyst Day, scheduled for July 15, 2021***

PRINCETON, N.J., July 01, 2021 (GLOBE NEWSWIRE) -- Oyster Point Pharma, Inc. (Nasdaq: OYST), today announced preclinical data in non-human primates and *in vitro* models evaluating OC-01 (varenicline) nasal spray against SARS-CoV-2 and the alpha and beta variants, the viruses that cause COVID-19 disease. Administration of OC-01 (varenicline) nasal spray, a highly selective nicotinic acetylcholine receptor agonist, protected rhesus macaques against SARS-CoV-2 nasal infection. The results were published on the preprint server bioRxiv (https://biorxiv.org/cgi/content/short/2021.06.29.450426v1).

“We believe this is the first *in vivo* and *in vitro* data illustrating a nicotinic acetylcholine receptor agonists’ potential to inhibit viral entry and disrupt replication of the SARS-CoV-2 virus and variants,” said Jeffrey Nau, PhD, MMS, president and CEO of Oyster Point. “We believe that OC-01 (varenicline) nasal spray has the potential to complement the current global vaccination strategy and prevent infection and reduce transmission of the SARS-CoV-2 virus with a mechanism of action that may have broad activity across multiple variants.”

On Day 1, using a viral infection model and following two administrations of 100 µl of OC-01 (varenicline) nasal spray (0.6 mg/ml varenicline) into each nostril, animals were challenged with a very high viral inoculum (approximately 70 thousand plaque-forming units) of active SARS-CoV-2, via both intranasal (nose) and intratracheal (lung) routes. Animals then received two additional administrations of OC-01 (varenicline) nasal spray into each nostril on Day 1, followed by four times daily for the following four days. Administration of OC-01 (varenicline) nasal spray resulted in inhibition of cellular entry and replication of SARS-CoV-2, illustrated by a decrease of detectable SARS-CoV-2 subgenomic RNA (sgRNA) by approximately 2 logs compared to controls with complete absence in all animals at 3 days and 5 days post-challenge. In control animals treated with the same lot of virus inoculum, nasal swabs reached a peak of approximately 10 million SARS-CoV-2 sgRNA copies within two days of viral challenge and were present throughout the course of the study. The absence of sgRNA indicates that the SARS-CoV-2 virus had not significantly infected nasal mucosa cells to start the transcription process of building new infectious virions. The absence of sgRNA following this very high viral inoculum also suggests the possibility of transmission may be substantially reduced after treatment with OC-01 (varenicline) nasal spray.

SARS-CoV-2 has been shown to predominantly enter the human body via nasal epithelial cells[1], specifically ciliated and mucous secreting cells of the nasal mucosa[2,3]. Therefore, the nasal cavity represents a highly susceptible mucosal surface for infection and amplification within the respiratory tree. The nasal cavity also allows for treatment with topical compounds that can be delivered in higher local concentrations with potentially lower systemic exposure that may not be achievable when administered as an oral tablet or IV infusion.

In a separate study, in collaboration with the Trudeau Institute, researchers evaluated the *in vitro* antiviral activity of varenicline against SARS-CoV-2 and SARS-CoV-2 alpha and beta variants using Calu-3 (human airway epithelial cells) and Caco-2 (colon epithelial cells) cell lines. “Varenicline has demonstrated potent antiviral activity against SARS-CoV-2 and variants, alpha and beta, in cell culture. The promising *in vitro* and *in vivo* data suggest a clinical path forward for OC-01, which could prove a potential treatment in preventing severe COVID-19 symptoms and the spread of infection. Further studies investigating the mechanism of action and its effect on other variants of concern, such as the gamma and delta variants are ongoing," said Priya Luthra, PhD, Trudeau Institute Principal Investigator.

Additionally, OC-02 (simpinicline), a highly selective nicotinic acetylcholine receptor agonist was evaluated for *in vitro* antiviral activity against the SARS-CoV-2 alpha variant using Calu-3 cell lines. Simpinicline demonstrated potent antiviral activity against the SARS-CoV-2 variants in cell culture with an IC_{50} of 0.04 µM. Further studies investigating the antiviral effect on other variants of concern are ongoing.

Given the results of both the *in vivo* and *in vitro* studies, OC-01 (varenicline) nasal spray and OC-02 (simpinicline) nasal spray warrant further investigation as an antiviral agent for pre-exposure prophylaxis, post-exposure prophylaxis, and/or prevention of transmission of SARS-CoV-2. Additional *in vivo and in vitro* studies are ongoing.

OC-01 (varenicline) nasal spray and OC-02 (simpinicline) nasal spray have not been proven safe or effective to prevent SARS-CoV-2 infection or treat COVID-19 in humans nor has OC-01 (varenicline) or OC-02 (simpinicline) nasal spray been approved for any use by the U.S. Food and Drug Administration (FDA). The Prescription Drug User Fee Act (PDUFA) target action date for OC-01 (varenicline) nasal spray is October 17, 2021, with a planned U.S. launch in the fourth quarter of 2021, if approved by the FDA.

Oyster Point Pharma plans to present additional data at the upcoming Oyster Point Analyst Day, planned for July 15, 2021. Please use the following link to register for the Analyst Day (https://media.rampard.com/20210715/).

About Oyster Point Pharma
Oyster Point Pharma is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of first-in-class pharmaceutical and biologic therapies to treat ophthalmic diseases.

About the Trudeau Institute
The Trudeau Institute, headquartered in Saranac Lake, N.Y., safeguards human health by combatting 21st-century global health crises, such as the rise of drug-resistant tuberculosis, COVID-19 and emerging pandemic viruses. Its roots can be traced to 1884, when Edward Livingston Trudeau launched the first American laboratory solely dedicated to tuberculosis research. Today, Trudeau scientists spearhead innovation by conducting urgent biomedical research on infectious disease and collaborating with national and international R&D partners to accelerate medical impact.

About OC-01 (varenicline) Nasal Spray

OC-01 (varenicline) nasal spray is a highly selective cholinergic agonist being developed as a multidose preservative-free nasal spray to treat the signs and symptoms of dry eye disease and neurotrophic keratopathy. Varenicline tartrate is a partial nicotinic acetylcholine receptor agonist of α4β2 and α4α6β2 receptors, a moderate α3β4 and α3α5β4 receptor agonist, and a full α7 receptor agonist. Varenicline has been hypothesized to form a complex with an epitope of the Severe Acute Respiratory Syndrome-related Coronavirus 2 (SARS-CoV-2) spike protein that may block binding to receptors important for cellular entry, resulting in the prevention of viral entry into tissues[1]. The administration of a nasal spray formulation of varenicline provides a high localized dose directly to the nasal mucosa, a frequent site of virus entry, replication and infection. Varenicline has been shown to inhibit viral entry and disrupt replication of SARS-CoV-2-alpha in an *in vivo* model and has been shown to have potent antiviral activity to SARS-CoV-2, SARS-CoV-2-alpha, and SARS-CoV-2-beta in *in vitro* assays. The Prescription Drug User Fee Act (PDUFA) target action date is October 17, 2021, with a planned U.S. launch of OC-01 (varenicline) nasal spray in this indication in the fourth quarter of 2021, if approved by the FDA. OC-01 (varenicline) nasal spray is an investigational new drug and has not been approved for any use in any country. The safety and efficacy of OC-01 (varenicline) nasal spray have not been established.

About OC-02 (simpinicline) Nasal Spray

OC-02 (simpinicline) nasal spray is a highly selective cholinergic agonist. Simipinicline citrate is a strong nicotinic acetylcholine receptor agonist of activity at the α4β2, α3β4, α3α5β4, and α4α6β2 receptors and weak agonist activity at the α7 receptor. OC-02 has been previously studied in two Phase 2b clinical trials for dry eye disease.

About the SARS-CoV-2 Virus
The Severe Acute Respiratory Syndrome-related Coronavirus 2 (SARS-CoV-2) is the virus responsible for coronavirus disease 2019 (COVID-19). This virus is from the Coronaviridae family that are broadly distributed among humans, other mammals, and birds. SARS-CoV-2 is a positive-sense single-stranded RNA virus.

Forward-Looking Statements
This press release contains “forward-looking statements” within the meaning of the Private Securities Litigation Reform Act of 1995 that reflect the current beliefs, expectations and assumptions of the Company regarding the future of the Company’s business, our future plans and strategies, regulatory approvals, clinical results, future financial condition and other future conditions. All statements other than statements of historical facts contained in this press release, including express or implied statements regarding product candidates, regulatory approvals, planned preclinical studies and clinical trials, expected results of preclinical or clinical trials, and their timing and likelihood of success, expected research and development costs, as well as plans and objectives of management for future operations, are forward-looking statements. The words “if approved,” “may,” “will,” “should,” “would,” “expect,” “plan,” “anticipate,” “could,” “intend,” “target,” “project,” “contemplate,” “believe,” “estimate,” “predict,” “potential” or “continue” or the negative of these terms or other similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: the timing or likelihood of regulatory filings and approvals for OC-01; the beneficial characteristics, safety, efficacy and therapeutic effects of OC-01; our plans relating to the further development and manufacturing of OC-01, including potential additional indications or disease areas to be evaluated and pursued; the timing of initiation of our future clinical trials; the uncertainties inherent in pharmaceutical research and development, including preclinical study and clinical trial results and additional analysis of existing data; the likelihood of our clinical trials demonstrating safety and efficacy of OC-01, and other positive results; our plans and potential for success relating to commercializing OC-01; our plans and ability to obtain or protect intellectual property rights, including extensions of existing patent terms where available; our ability to recruit and retain key personnel needed to develop and commercialize our product candidates, if approved, and to grow our company; existing regulations and regulatory developments in the United States and other jurisdictions; our continued reliance on third parties to conduct additional preclinical studies and clinical trials of our product candidates, and for the manufacture of our product candidates for preclinical studies and clinical trials; the accuracy of our estimates regarding expenses, future revenue, capital requirements and needs for additional financing; our financial performance; market conditions; the sufficiency of our existing capital resources to fund our future operating expenses and capital expenditure requirements; and other risks described in the “Risk Factors” section included in our public filings that we have made and will make with the Securities and Exchange Commission (SEC). The Company is providing the information in this press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

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3. Gallo, O., Locatello, L. G., Mazzoni, A., Novelli, L., & Annunziato, F. (2020). The central role of the nasal microenvironment in the transmission, modulation, and clinical progression of SARS-CoV-2 infection. Mucosal immunology, 1-12.

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