Mallinckrodt Supports Investigator-Initiated Study at Massachusetts General Hospital to Assess Effectiveness of Inhaled Nitric Oxide in Patients with Severe Acute Respiratory Distress Syndrome Due to COVID-19

April 30, 2020

- More than 170 U.S. hospitals have reported using INOmax® (nitric oxide) gas, for inhalation, to treat COVID-19 lung complications -

STAINES-UPON-THAMES, United Kingdom, April 30, 2020 /PRNewswire/ -- Mallinckrodt plc (NYSE: MNK), a global biopharmaceutical company, announced today that it is supporting an investigator-initiated clinical study at Massachusetts General Hospital evaluating the potential benefits of inhaled nitric oxide as a treatment for pulmonary complications in patients infected with COVID-19. Mallinckrodt's support to Massachusetts General Hospital includes providing funding as well as INOmax® (nitric oxide) gas, for inhalation, to facilitate the study.

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The study is titled "Inhaled Nitric Oxide Gas Therapy in Mechanically Ventilated Patients with Severe Acute Respiratory Syndrome in COVID-19."

"Data suggest that inhaled nitric oxide may have an important role in helping patients with acute respiratory distress syndrome (ARDS) to achieve normal oxygen levels in the blood," said **Lorenzo Berra, M.D., Medical Director of Respiratory Care at Massachusetts General Hospital**. "The trial we are conducting will help us gain critical insights into the potential effectiveness of INOmax in treating ARDS in critically ill COVID-19 patients."

The primary focus of the study is to assess the potential efficacy of inhaled nitric oxide to rapidly reverse hypoxemia (abnormally low oxygen levels in the blood) in patients with severe COVID-19 lung complications . Specifically, it will determine the difference in oxygenation in patients after 48 hours of treatment. Secondary objectives include evaluating the time it takes for patients who are breathing air to reach normoxia (normal oxygen levels in the blood) for at least 24 hours; the proportion of patients who achieve normoxia during the first 28 days after enrollment; and the patient survival rate at 28 days and 90 days, among other objectives.

"Patients around the world are in need of science-based therapies that can effectively fight this life-threatening disease, and Mallinckrodt is committed to assisting health providers and government agencies to research and identify possible solutions to help relieve this global crisis," said **Steven Romano, M.D., Executive Vice President and Chief Science Officer at Mallinckrodt**. "We are extremely pleased to support Massachusetts General Hospital in these research efforts to potentially bring a new therapeutic option to physicians and patients who need it most."

The trial initiation follows Mallinckrodt's earlier announcement of a research project in Canada. On April 1, Mallinckrodt and Novoteris LLC, a clinical stage medical device and pharmaceutical developer, announced that the companies received approval from Health Canada to begin a pilot trial of high-dose inhaled nitric oxide therapy to treat the COVID-19 infection and associated lung complications. Enrollment is expected to begin in the coming days.

More than 170 hospitals and health systems in the U.S. have reported using INOmax as an experimental treatment for pulmonary complications of COVID-19 patients.[1] The current trial will enable formal data collection in a structured study of the efficacy and safety of inhaled nitric oxide in patients with pulmonary complications of COVID-19.

Mallinckrodt encourages hospitals to contact the company's Customer Care center 1-877-566-9466 with any questions related to INOmax. The Customer Care team is available 24 hours a day, seven days a week to respond to inquiries.

INOmax has been on the market in the U.S. since 2000 and is indicated for the treatment of term and near-term neonates with hypoxic respiratory failure associated with pulmonary hypertension. The safety and efficacy of INOmax to treat COVID-19 infections and associated lung complications have not been established by the U.S. Food and Drug Administration.

COVID-19 is a respiratory illness that can spread from person to person. It is caused by a novel coronavirus. Patients with COVID-19 may have mild to severe respiratory illness that can include symptoms such as cough, fever and shortness of breath.[2] In severe cases, COVID-19 can cause ARDS – a disorder in which fluid leaks into the lungs, making breathing difficult or impossible – and can lead to multi-organ failure and sometimes death.[2,3]

INDICATION

INOmax® (nitric oxide) gas, for inhalation, is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with hypoxic respiratory failure associated with clinical or echocardiographic evidence of pulmonary hypertension in conjunction with ventilatory support and other appropriate agents.

IMPORTANT SAFETY INFORMATION

- INOmax is contraindicated in the treatment of neonates dependent on right-to-left shunting of blood.
- Abrupt discontinuation of INOmax may lead to increasing pulmonary artery pressure and worsening oxygenation.
- Methemoglobinemia and NO_2 levels are dose dependent. Nitric oxide donor compounds may have an additive effect with INOmax on the risk of developing methemoglobinemia. Nitrogen dioxide may cause airway inflammation and damage to lung tissues.
- In patients with pre-existing left ventricular dysfunction, INOmax may increase pulmonary capillary wedge pressure leading to pulmonary edema.
- Monitor for PaO_2, inspired NO_2, and methemoglobin during INOmax administration.
- INOmax must be administered using a calibrated FDA-cleared Nitric Oxide Delivery System.

Please see Full Prescribing Information.

ABOUT MALLINCKRODT
Mallinckrodt is a global business consisting of multiple wholly owned subsidiaries that develop, manufacture, market and distribute specialty pharmaceutical products and therapies. The company's Specialty Brands reportable segment's areas of focus include autoimmune and rare diseases in specialty areas like neurology, rheumatology, nephrology, pulmonology and ophthalmology; immunotherapy and neonatal respiratory critical care therapies; analgesics and gastrointestinal products. Its Specialty Generics reportable segment includes specialty generic drugs and active pharmaceutical ingredients. To learn more about Mallinckrodt, visit www.mallinckrodt.com.

Mallinckrodt uses its website as a channel of distribution of important company information, such as press releases, investor presentations and other financial information. It also uses its website to expedite public access to time-critical information regarding the company in advance of or in lieu of distributing a press release or a filing with the U.S. Securities and Exchange Commission (SEC) disclosing the same information. Therefore, investors should look to the Investor Relations page of the website for important and time-critical information. Visitors to the website can also register to receive automatic e-mail and other notifications alerting them when new information is made available on the Investor Relations page of the website.

CAUTIONARY STATEMENTS RELATED TO FORWARD-LOOKING STATEMENTS
This release includes forward-looking statements concerning inhaled nitric oxide ("iNO") and the Company's iNO product, including statements with regard to potential regulatory developments, the potential impact of iNO on patients and anticipated benefits associated with its use. The statements are based on assumptions about many important factors, including the following, which could cause actual results to differ materially from those in the forward-looking statements: satisfaction of regulatory and other requirements; actions of regulatory bodies and other governmental authorities; changes in laws and regulations; issues with product quality, manufacturing or supply, or patient safety issues; and other risks identified and described in more detail in the "Risk Factors" section of Mallinckrodt's most recent Annual Report on Form 10-K and other filings with the SEC, all of which are available on its website. The forward-looking statements made herein speak only as of the date hereof and Mallinckrodt does not assume any obligation to update or revise any forward-looking statement, whether as a result of new information, future events and developments or otherwise, except as required by law.

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References

[1] Mallinckrodt, Data on File April 28, 2020.

[2] Centers for Disease Control and Prevention Fact Sheet. What you need to know about coronavirus disease 2019 (COVID-19).

[3] Matthay MA, Aldrich JM, Gotts, JE. Treatment for severe acute respiratory distress syndrome from COVID-19. *Lancet Respir Med*. 2020. Published Online March 20, 2020. https://doi.org/10.1016/S2213-2600(20)30127-2.


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