



Mallinckrodt Evaluates the Potential Role for Inhaled Nitric Oxide to Treat COVID-19 Associated Lung Complications, Engages with Scientific, Governmental and Regulatory Agencies

March 12, 2020

STAINES-UPON-THAMES, United Kingdom, March 12, 2020 /PRNewswire/ -- [Mallinckrodt plc](#) (NYSE: MNK), a global biopharmaceutical company, today commented that it is currently evaluating the limited published evidence suggesting a potential role for inhaled nitric oxide ("iNO") as a supportive measure in treating those patients infected with coronavirus (SARS-CoV-2) and having associated pulmonary complications. The company has engaged with the U.S. Food and Drug Administration (FDA), the National Institutes of Health (NIH) and the Biomedical Advanced Research and Development Authority (BARDA) on this matter; however, the safety and efficacy of iNO for pulmonary complications associated with coronavirus have not been established.

Mallinckrodt markets iNO as INOmax® (nitric oxide) gas for inhalation in the U.S. for the treatment of term and near-term neonates with hypoxic respiratory failure associated with pulmonary hypertension. Please see Important Safety Information below.

While nitric oxide has not been specifically studied or used to treat COVID-19, *in vitro* it has demonstrated an inhibitory effect on the replication cycle of severe acute respiratory syndrome-related coronavirus (SARS-CoV).¹ In another study, investigators utilized iNO in the treatment of six patients infected with SARS-CoV. This study compared the outcomes of the six patients treated with iNO to eight controls. Improvements in blood oxygenation, a reduction in supplemental oxygen and a reduction in the amount of ventilator support were achieved.²

A potential clinical manifestation of infection with many respiratory viruses (such as coronaviruses or influenzas) is acute respiratory distress syndrome (ARDS) - a disorder in which fluid leaks into the lungs, making breathing difficult or impossible. iNO has been evaluated in randomized controlled trials, both in pediatric and adult patients with ARDS.³⁻⁷ In one study, iNO elicited a partially dose dependent improvement in blood oxygenation and decreased pulmonary artery pressure.³ In a second trial, evaluating pediatric ARDS patients, improvements were found in the composite measure of days alive or free of ventilator support at day 28 of the trial (the last day evaluated).⁸ There have been other trials evaluating iNO in the context of ARDS, which have demonstrated mixed results.⁹

In recent days, the company has submitted information to the NIH regarding the potential to evaluate iNO in ARDS, informed BARDA of the ongoing evaluation in this area and is in early discussions with the FDA on the potential to submit a pre-Investigational New Drug (IND) package in support of the potential use of iNO in coronavirus-associated ARDS.

"Mallinckrodt is evaluating the limited data presently available on inhaled nitric oxide as a supportive measure for treating coronavirus-associated lung complications," said Steve Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt. "We are in ongoing discussions with scientific, regulatory and governmental organizations regarding the potential use of iNO in assisting with this global emergency, and are committed to determining whether iNO has a benefit for those diagnosed with COVID-19. We will share updates as information becomes available."

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 NO₂ 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 PaO₂, inspired NO₂, 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.

CONTACTS

For Trade Media Inquiries

Caren Begun
Green Room Communications
201-396-8551
caren@greenroompr.com

For Financial/Dailies Media Inquiries

Jim Heins
H+K Strategies
212-885-0463
jim.heins@hkstrategies.com

Investor Relations

Daniel J. Speciale, CPA
Vice President, Investor Relations and IRO
314-654-3638
daniel.speciale@mnk.com

Government Affairs

Mark Tyndall
Senior Vice President, Government Affairs
202-383-0090
mark.tyndall@mnk.com

Mallinckrodt, the "M" brand mark and the Mallinckrodt Pharmaceuticals logo are trademarks of a Mallinckrodt company. Other brands are trademarks of a Mallinckrodt company or their respective owners. ©2020 Mallinckrodt. US-2000421 03/20

References

1. Akerstrom S et. Al. Nitric oxide inhibits the Replication Cycle of Severe Acute Respiratory Syndrome Coronavirus. J Virol 2005; 79(3):1966-9.
2. Chen L. Inhalation of nitric oxide in the treatment of acute respiratory syndrome: a rescue trial in Beijing. Clinical Infectious Diseases 2004; 39(10):1531-5.
3. Gerlach H, Keh D, Semmerow A, et al. Dose-response characteristics during long-term inhalation of nitric oxide in patients with severe acute respiratory distress syndrome: a prospective, randomized, controlled study. Am J Respir Crit Care Med. 2003;167(7):1008-15.
4. Payen D, Valle B. Results of the French prospective multicentric randomized double-blind placebo-controlled trial on inhaled nitric oxide (NO) in ARDS. Intensive Care Med. 1999;25(1432-1238 (Electronic)):S166.
5. Dellinger RP, Zimmerman JL, Taylor RW, et al. Effects of inhaled nitric oxide in patients with acute respiratory distress syndrome: results of a randomized phase II trial. Inhaled Nitric Oxide in ARDS Study Group. Crit Care Med. 1998;26(1):15-23.
6. Michael JR, Barton RG, Saffle JR, et al. Inhaled nitric oxide versus conventional therapy: effect on oxygenation in ARDS. Am J Respir Crit Care Med. 1998;157(5 Pt 1):1372-80.
7. Troncy E, Collet JP, Shapiro S, et al. Inhaled nitric oxide in acute respiratory distress syndrome: a pilot randomized controlled study. Am J Respir Crit Care Med. 1998;157(5 Pt 1):1483-8.
8. Bronicki RA, Fortenberry J, Schreiber, M, Checchia PA, Anas NG. Multicenter randomized controlled trial of inhaled nitric oxide for pediatric acute respiratory distress syndrome. The Journal of Pediatrics 2015. 66(2):365-9.
9. Hunt JL, Bronicki RA, Anas N. Role of inhaled nitric oxide in the management of severe acute respiratory distress syndrome. Frontiers in Pediatrics. 2016;4:1-7.

 View original content to download multimedia:<http://www.prnewswire.com/news-releases/mallinckrodt-evaluates-the-potential-role-for-inhaled-nitric-oxide-to-treat-covid-19-associated-lung-complications-engages-with-scientific-governmental-and-regulatory-agencies-301022189.html>

SOURCE Mallinckrodt Pharmaceuticals