



Mallinckrodt Presents Data Evaluating INOmax® (Nitric Oxide) Gas, for Inhalation in a Phase 4 Observational Registry in Neonates with Pulmonary Hypertension at the Pediatric Academic Societies (PAS) 2021 Virtual Meeting

April 30, 2021

- Full results presented for Phase 4 observational registry, which ended early upon achievement of statistical significance for non-inferiority in premature neonates compared to term and near-term neonates at planned interim analysis -

DUBLIN, April 30, 2021 /PRNewswire/ -- [Mallinckrodt plc](#) (OTCMKTS: MNKKQ), a global biopharmaceutical company, today announced that data from its Phase 4 observational registry comparing the safety and effectiveness of INOmax® (nitric oxide) gas, for inhalation, in term and near-term (TNT) neonates to that in preterm (PT) neonates with pulmonary hypertension (PH) will be presented in a poster at The Pediatric Academic Societies (PAS) 2021 Virtual Meeting. The poster can be accessed [here](#) on the company's website. The safety and efficacy of INOmax in premature neonates has not been evaluated by the U.S. Food and Drug Administration.



INOmax has been on the market in the U.S. since 2000 and 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. Please see Important Safety Information below.

The primary outcome measure of the registry was the number of PT neonates and TNT neonates with a significant response to INOmax, which was defined as at least a 25 percent improvement (decrease) from baseline in oxygenation index or surrogate oxygenation index (OI/SOI) during INOmax treatment. A total of 50 (90.9 percent) PT and 75 (88.2 percent) TNT neonates achieved a ≥25 percent decrease in OI/SOI during treatment with INOmax. Efficacy in the PT group demonstrated non-inferiority (95 percent confidence interval: 0.0267 [-0.0333, 0.0868], with a pre-defined margin of -0.1452). In addition, the proportion of neonates with ≥25 percent decrease in OI/SOI was similar across severity groups with no significant difference in time to improvement between groups.¹

"These registry findings help expand our understanding of a potential role of inhaled nitric oxide therapy in preterm infants with hypoxic respiratory failure with pulmonary hypertension," **said study author Leif D. Nelin, M.D., Division Chief of Neonatology at Nationwide Children's Hospital.**

Persistent pulmonary hypertension of the newborn (PPHN) is a serious and sometimes fatal cardiorespiratory complication of the transition to extra-uterine life.^{2,3} The registry trial was conducted to examine the utility of INOmax in pre-term neonates. Due to the seriousness of the condition, a randomized controlled trial cannot be conducted in the pre-term neonate population.

Overall, 21 adverse events of special interest were reported in 17 patients, all of which were classified as serious events, and no serious adverse events were attributed to the study drug.

"After ending this registry much earlier than anticipated last year based on positive findings, Mallinckrodt is extremely pleased to be able to share these important data with the healthcare community and add to the body of research and real-world data for this vulnerable patient population," **said Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt.**

About the Observational Registry

- The **Registry Evaluating Premature and Term and Near-Term Neonates with Pulmonary Hypertension Receiving Inhaled Nitric Oxide (PaTTeRN)** was a multicenter, prospectively defined, observational registry study that evaluated the use of INOmax to treat pulmonary PH in premature neonates (27 to less than 34 weeks gestational age) and term and near-term neonates (34 to 40 weeks gestational age).
- In the 11-day study period, a total of 140 neonates (PT, n=55; TNT, n=85) were enrolled across 30 sites in the United States.
- The primary outcome measure compared the incidence of subjects with at least a 25 percent improvement (decrease) from baseline in OI or SOI during the INOmax treatment period in pre-term versus term and near-term neonates with PH.

- Secondary efficacy endpoints included:
 - The incidence of subjects with at least a 25 percent improvement in OI/SOI in each severity group of mild, moderate and severe
 - The time to response to INOmax up to 96 hours for each severity and age group
 - Evaluation of 25 percent improvement in OI/SOI with univariate and multivariate logistic regressions for baseline factors: age and severity group, disease subtype, weight, race, gender
 - The incidence of partial responders (<25 percent improvement in OI/SOI) and non-responders (<5 percent improvement in OI/SOI) summarized by age group and by each severity group within each age group
- Patients were classified as mild, moderate or severe based on a primary measure of OI or a secondary measure of SOI for hypoxic respiratory failure (HRF) severity:
 - Mild: OI <16 or SOI <10
 - Moderate: OI value 16 to 25 or SOI value 10 to 15
 - Severe: OI >25 or SOI >15
- Patients were evaluated for response to INOmax and safety during a treatment period of up to 96 hours ± 12 hours and a safety follow-up through 7 days (for a total of up to 11 days) or to hospital discharge, whichever came first

More information about the trial can be found [here](#).

Study Limitations

The study was a prospective observational registry that collected real world data that described INOmax nitric oxide gas use in clinical practice. As an observational study it did not utilize placebo. Hence, some of the improvement observed in the study could be due to factors other than treatment with INOmax. Similarly, without placebo control it is not possible to understand the magnitude to which patients who experienced limited response to inhaled nitric oxide would have otherwise decompensated without this treatment.

About Persistent Pulmonary Hypertension of the Newborn (PPHN)

PPHN is a serious and sometimes fatal cardiorespiratory complication of the transition to extra-uterine life.^{2,3} PPHN is a clinical syndrome associated with various neonatal cardiorespiratory diseases, including meconium aspiration, respiratory distress syndrome (hyaline membrane disease), congenital heart disease and congenital hernia.² Despite the diversity of causes, marked pulmonary vasoconstriction is the central pathophysiologic feature of PPHN.⁴ The most significant hemodynamic feature in neonates with severe hypoxia is a pulmonary-to-systemic pressure imbalance.⁵ Treatment in these neonates is directed toward lowering the pulmonary vascular pressure and supporting the systemic circulation.^{2,4}

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 the clinical data generated in the study described above. 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


Investor Relations

Daniel J. Speciale, CPA
Vice President, Finance and Investor Relations Officer
314-654-3638
daniel.speciale@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. ©2021 Mallinckrodt. US-2000338 04/21

References

- ¹ Nelin L, Kinsella J, Courtney S, Pallotto E, Tarau E, Potenziano J. Use of Inhaled Nitric Oxide in Preterm vs Term/Near-Term Neonates With Pulmonary Hypertension: Results of the PaTTERN Registry Study. Presented at: Pediatric Academic Societies Annual Meeting; May 1, 2021.
- ² Nair J, Lakshminrusimha S. Update on PPHM: Mechanisms and treatment. *Semin Perinatol*. 2014;38(2):78-91.
- ³ Clark RH. The epidemiology of respiratory failure in neonates born at an estimated gestational age of 34 weeks or more. *J Perinatol*. 2005;25(4):251-257.
- ⁴ Wedgwood S, Steinhorn RH, Lakshminrusimha S. Optimal oxygenation and role of free radicals in PPHN. *Free Radical Biology and Medicine*. 2019;142:97-106.
- ⁵ Lakshminrusimha S. The pulmonary circulation in neonatal respiratory failure. *Clin Perinatol*. 2012;39(3):655-683.

 View original content to download multimedia: <http://www.prnewswire.com/news-releases/mallinckrodt-presents-data-evaluating-inomax-nitric-oxide-gas-for-inhalation-in-a-phase-4-observational-registry-in-neonates-with-pulmonary-hypertension-at-the-pediatric-academic-societies-pas-2021-virtual-meeting-301281332.html>

SOURCE Mallinckrodt plc