Mallinckrodt Announces Encouraging Interim Analysis Results in Phase 4 Registry of INOmax® (Nitric Oxide) Gas for Inhalation for Pulmonary Hypertension in Neonates

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-- Observational registry (at midway point) with retrospective data collection provides preliminary evaluation of premature versus term and near-term neonates with pulmonary hypertension receiving inhaled nitric oxide --

STAINES-UPON-THAMES, United Kingdom, May 6, 2019 /PRNewswire/ -- Mallinckrodt plc (NYSE: MNK), a leading global specialty pharmaceutical company, today announced preliminary results of a planned interim analysis from the company's Phase 4 registry assessing the use of INOmax® (nitric oxide) gas, for inhalation, for premature (27 to less than 34 weeks gestational age) neonates versus term and near-term neonates (34 weeks and greater gestational age) with pulmonary hypertension (PH).

The primary outcome measure compares the incidence of mechanically ventilated subjects with PH who achieve at least a 25 percent improvement in Oxygenation Index (OI) from baseline, or Surrogate Oxygenation Index (SOI) for subjects who are not ventilated, between gestation age groups. OI is commonly used to evaluate the severity of hypoxic respiratory failure (HRF) in neonates with PH.

The planned interim analysis occurred at the approximate midway point of enrollment (n=31 in the premature arm vs. n=56 in the term and near-term arm). The preliminary analysis found that, at this juncture in the study, approximately 86% of both cohorts showed a 25% or greater improvement in OI or SOI during the treatment period. The safety and efficacy of INOmax nitric oxide gas for treating HRF in premature neonates with PH has not been evaluated by the U.S. Food and Drug Administration (FDA).

"We are encouraged to see the results of the interim analysis for this patient population and look forward to learning more as this retrospective, observational registry enrollment progresses," said **Steven Romano, M.D., Executive Vice President and Chief Scientific Officer at Mallinckrodt**. "Mallinckrodt is focused on making a difference for underserved patients, including those with critical conditions like neonates with HRF."

INOmax nitric oxide gas is approved by the FDA for use to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term neonates (at 34 weeks and greater gestational age) with HRF associated with clinical or echocardiographic evidence of PH in conjunction with ventilatory support and other appropriate agents.

Study Limitations

The current study is a prospective observational registry that collects real world data that describes how INOmax nitric oxide gas is being used in clinical practice. As an observational study it does not utilize placebo or active control groups as comparators. Hence, some of the improvement observed in the current 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 the Study

The Phase 4 registry is titled "Multicenter, Prospectively Defined Observational Registry With Retrospective Data Collection, Evaluating Premature and Term-Near-Term Neonates With Pulmonary Hypertension Receiving Inhaled Nitric Oxide via Invasive or Noninvasive Ventilator Support at U.S. Centers" or the "Registry Evaluating **P**remature **a**nd **T**erm-Near-**Ter**m **N**eonates With Pulmonary Hypertension Receiving Inhaled Nitric Oxide (PaTTerN)" trial. Data collected from this registry can help increase understanding of the potential utility of inhaled nitric oxide for treating PH and improving oxygenation in pre-term neonates with HRF associated with PH compared to term and near-term neonates with HRF associated with PH.

Targeted enrollment for this study is 168 patients. The primary outcome measure compares the incidence of subjects with at least a 25% improvement in Oxygenation Index or Surrogate Oxygenation Index (for subjects who are not mechanically ventilated), compared to baseline and summarized by gestation age group. Study completion is expected by 2022.

No drug-related significant safety issues have been identified in this observational, retrospective data to date.

More information on the study can be found here on clinicaltrials.gov.

About Persistent Pulmonary Hypertension of the Newborn (PPHN)
PPHN is a serious and sometimes fatal cardiorespiratory complication of the transition to extra-uterine life.[1] 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. Despite the diversity of causes, marked pulmonary vasoconstriction is the central pathophysiologic feature of PPHN. The most significant hemodynamic feature in neonates with severe hypoxia is a pulmonary-to-systemic pressure imbalance. Treatment in these neonates is directed toward lowering the pulmonary vascular pressure and supporting the systemic circulation.

About INOmax®
In the U.S., INOmax is indicated to improve oxygenation and reduce the need for extracorporeal membrane oxygenation in term and near-term (>34 weeks gestation) neonates with HRF 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, methemoglobin, and inspired NO_2 during INOmax administration.
- INOmax must be administered using a calibrated, FDA-cleared INOmax DS_{IR}® Nitric Oxide Delivery System.

Please see U.S. 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; and analgesics. Its Specialty Generics and Amitiza® reportable segment includes specialty generic drugs, active pharmaceutical ingredients and AMITIZA (lubiprostone). 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 the company's Phase 4 registry related to INOmax for premature neonates, including expectations with regard to the registry, future research plans and the potential impact on patients. 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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[1] Data on file. Mallinckrodt Pharmaceuticals.

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