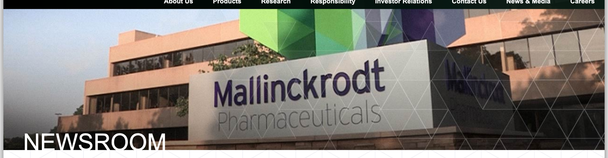

NEWSROOM

News Release

Mallinckrodt Licenses Inhaled Xenon Gas Therapy Development Product

-- Drug-device combination therapy for inhaled pharmaceutical-grade xenon gas under investigation to lessen brain damage, improve survival and function in patients suffering cardiac arrest --

-- FDA Special Protocol Assessment approved for Phase 3 trial to begin early 2018; FDA Orphan Drug Designation granted --

-- NeuroprotoXeon to receive upfront payment of $10 million from Mallinckrodt from cash on hand; agreement includes additional payments of up to $25 million dependent on development, regulatory and sales milestones --

-- Mallinckrodt anticipates dilution of $0.10 to $0.15 to adjusted diluted earnings per share for the rest of 2017, modestly lower in 2018 --

STAINES-UPON-THAMES, United Kingdom, Oct. 2, 2017 /PRNewswire/ -- Mallinckrodt plc (NYSE:MNK) today announced it has entered into a licensing agreement for development and commercialization of NeuroprotoXeon's investigational, pharmaceutical-grade xenon gas for inhalation therapy being evaluated to improve survival and functional outcomes for patients resuscitated after a cardiac arrest. If approved, xenon gas for inhalation will expand Mallinckrodt's portfolio of hospital drug-device combination products providing therapies for critically ill patients.

Under terms of the agreement, later today Mallinckrodt will pay $10 million upfront with cash on hand to reimburse NeuroprotoXeon for certain product development costs, and gains exclusive rights to commercialize the therapy, if approved, in the U.S., Canada, Japan and Australia. Mallinckrodt will make additional payments of up to $25 million dependent on achievement of clinical, regulatory and sales milestones as well as a tiered, net-sales-based royalty. NeuroprotoXeon will continue to be responsible for the cost of development and will manage the development of the product in collaboration with Mallinckrodt.

Approximately 500,000 people in the U.S. experience cardiac arrest every year[1], more than half of whom are over 65. When a patient's heart stops beating, death can occur within minutes but today ~35%-40% of these patients are revived and their heartbeat and blood circulation returns. However, even when successfully resuscitated, only 30%-35% of these resuscitated patients survive to leave the hospital[2]. Among survivors, coma or brain damage, including impairment of motor function, memory and cognition, are common. Improving survival and reducing brain damage and impairment is of paramount importance for these individuals and their families. And it's critically important for the healthcare system as well, given that the average cost of care in the U.S. -- from the cardiac arrest through the 12 months following -- is roughly $100,000 per patient[3].

Rates of resuscitation following cardiac arrest have risen modestly over time, but physicians say they still are not as high as they could or should be. The problem is beginning to be addressed in developed markets with campaigns focused on cardiopulmonary resuscitation training and programs to install defibrillators in workplaces, arenas, retail stores and even public transportation. But another equally serious problem exists. Even when patients are successfully resuscitated, their outcomes are frequently still not positive, and post-arrest care and management continues to be an area of very high unmet medical need.

"Only about a third of patients resuscitated following cardiac arrest survive to leave the hospital," said **Dr. Steve Romano, Executive Vice President and Chief Scientific Officer**, "and survivors still have significant rates of coma and long-term functional or cognitive disability. The standard of care for treatment of these patients includes 24 hours of targeted temperature management, or hypothermia therapy, but there are currently no specific approved pharmacologic treatments available for use. The Phase 3 xenon gas for inhalation registration trial that will begin in early 2018 is designed to confirm a potential clinical benefit associated with the positive biomarker outcome as demonstrated on magnetic resonance imaging (MRI) scans of patients treated with hypothermia therapy plus xenon gas for inhalation that was seen in a Phase 2b study. Those results – published in the March 2016 edition of the *Journal of the American Medical Association* (JAMA) – showed a measurable reduction in brain damage. The Phase 3 trial, being conducted under an FDA Special Protocol Agreement, or SPA, will seek to measure the clinical benefit of xenon gas for inhalation in terms of improved 30-day survival and improved functional outcomes."

About the Phase 2b Study and the Possible Mechanism of Action of Xenon Gas for Inhalation

The Phase 2b study, a randomized, single-blind, clinical drug trial, studied 110 comatose patients who had experienced cardiac arrest. Patients were randomly assigned to receive 24 hours of standard-of-care hypothermia therapy, alone or 24 hours of hypothermia therapy plus inhaled xenon gas. The primary endpoint was reduction of cerebral white matter damage (brain damage) in areas associated with several important cognitive functions, as assessed by MRI.

The result was that MRI scans showed a statistically significant lowering of brain damage ($p = 0.006$) in patients treated with xenon gas for inhalation plus hypothermia. Although the study was underpowered for clinical endpoints and showed no statistically significant difference in mortality rates ($p = 0.053$) or neurological outcomes at six months in the overall population, subsequent analysis showed potentially intriguing positive outcomes in a subset population. In patients resuscitated within 30 minutes (roughly 90% of the overall study population), those treated with hypothermia therapy plus xenon gas for inhalation had improved mortality and the improved functional and cognitive outcome. The Phase 3 trial, designed under an FDA SPA, will study these clinical endpoints at 30 days in this targeted population – patients resuscitated within 30 minutes – in approximately 1,400 patients.

In patients who have had cardiac arrest, low blood flow and poor oxygenation of brain tissue may lead to a number of changes including the opening of calcium channels, which are known to contribute to neuronal injury and death, leading to brain damage. Xenon gas for inhalation binds to a receptor that can regulate these calcium channels and potentially mitigate these negative neuronal effects.

"If the planned Phase 3 study is successful and the biological effect seen in the Phase 2 study translates to clinical impact, we believe xenon gas for inhalation has the potential to change treatment paradigms and increase adoption of the therapy in a population of resuscitated cardiac arrest patients," said Dr. Romano.

The Special Protocol Assessment that has been approved by the FDA allows for an interim analysis at 50% of trial completion of the primary endpoint follow up, and if the primary and secondary endpoints are positive at that review the trial would be halted for success. If the primary or secondary endpoints are futile at that point, the trial will be stopped for futility. Assuming full completion of the trial, Mallinckrodt expects the regulatory submission to be a drug and delivery device combination and anticipates receiving U.S. regulatory approval in late 2020.

U.S. regulatory approval is the first priority, but Mallinckrodt is also evaluating regulatory strategies for market entry in the remaining countries aligned with its existing footprint where it has commercialization rights. The device for the trial and for any commercialized product will be supplied by Penion and Praxair will supply the pharmaceutical grade xenon gas for inhalation under supply agreements with NeuroprotoXeon.

Ron Lloyd, Executive Vice President and President of Hospital Therapies for Mallinckrodt, said, "Xenon gas for inhalation addresses a critical unmet need and is a natural fit with Mallinckrodt's specialty brands portfolio, where we can leverage our unique drug-delivery expertise and existing hospital infrastructure to commercialize this product. This product can add value to patients and also help us continue to deliver on our growth strategy for the hospital business."

Bill Bunn, NeuroprotoXeon Chief Executive Officer, said, "We are excited by the partnership with Mallinckrodt and we believe they are the ideal partner given their pharmaceutical gas and drug-device experience, as well as their broad service and technical support infrastructure. We look forward to working closely with Mallinckrodt in bringing this important therapy to the market so patients having a cardiac arrest may have better survival rates and neurological outcomes."

Financial Considerations, Closing and Commercialization

Under terms of the agreement, NeuroprotoXeon will receive an upfront payment of $10 million in cash on hand from Mallinckrodt, with potential additional payments of up to $25 million dependent on developmental, regulatory and sales milestones. In addition, NeuroprotoXeon will receive tiered royalties on applicable worldwide product sales and a transfer price for commercial product supply.

Mallinckrodt expects dilution of $0.10 to $0.15 to GAAP[(1)] earnings per share and adjusted diluted earnings per share for the remainder of 2017, with slightly lower dilution in 2018. Note that the majority of the dilution to 2017 will come from the upfront, one-time consideration, which the company will not remove for non-GAAP reporting purposes. The transaction closing will be concurrent with the upfront payment being paid later today.

If approved, Mallinckrodt expects xenon gas for inhalation to be commercialized by the company's existing sales organization. At launch, patient access to this unique treatment option would also be supported and enhanced by the company's strong relationships with hospital networks, insurance companies and group purchasing organizations. Mallinckrodt's existing infrastructure of clinical and medical affairs experts will also support both approval and launch of the product.

About Xenon Gas for Inhalation

Xenon is a noble gas that has been used safely as an inhaled therapy in several studies to date. In cardiac arrest, calcium channels in the brain can get over-activated, causing neuronal damage and cell death. Xenon binds to N-methyl-D-aspartate receptors through a unique glycine-binding mechanism and can help regulate the flow of ions through the calcium channels. By mitigating neuronal damage and cell death, xenon may be able to reduce time in coma, lower mortality rates and improve cognitive and motor functions.

About Mallinckrodt

Mallinckrodt is a global business that develops, manufactures, markets and distributes specialty pharmaceutical products and therapies. 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 hemostasis products. The company's core strengths include the acquisition and management of highly regulated raw materials and specialized chemistry, formulation and manufacturing capabilities. The company's Specialty Brands segment includes branded medicines and its Specialty Generics segment includes specialty generic drugs, active pharmaceutical ingredients and external manufacturing. 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

Statements in this document that are not strictly historical, including statements regarding future financial condition and operating results, economic, business, competitive and/or regulatory factors affecting Mallinckrodt's businesses and any other statements regarding events or developments that we believe or anticipate will or may occur in the future, may be "forward-looking" statements within the meaning of the Private Securities Litigation Reform Act of 1995, and involve a number of risks and uncertainties.

There are a number of important factors that could cause actual events to differ materially from those suggested or indicated by such forward-looking statements and you should not place undue reliance on any such forward-looking statements. These factors include risks and uncertainties related to, among other things: general economic conditions and conditions affecting the industries in which Mallinckrodt operates; the commercial success of Mallinckrodt's products; Mallinckrodt's ability to realize anticipated growth, synergies and cost savings from transactions (including the NeuroprotoXeon transaction); conditions that could necessitate an evaluation of Mallinckrodt's goodwill and/or intangible assets for possible impairment; changes in laws and regulations; Mallinckrodt's ability to successfully integrate acquisitions of operations, technology, products and businesses generally and to realize anticipated growth, synergies and cost savings (including with respect to the NeuroprotoXeon transaction); Mallinckrodt's ability to successfully develop or commercialize new products; Mallinckrodt's ability to protect intellectual property rights; Mallinckrodt's ability to receive procurement and production quotas granted by the U.S. Drug Enforcement Administration; customer concentration; Mallinckrodt's reliance on certain individual products that are material to its financial performance; cost containment efforts of customers, purchasing groups, third-party payers and governmental organizations; the reimbursement practices of a small number of public or private insurers; pricing pressure on certain of Mallinckrodt's products due to legal changes or changes in insurers' reimbursement practices resulting from recent increased public scrutiny of healthcare and pharmaceutical costs; limited clinical trial data for H.P. Acthar® Gel; complex reporting and payment obligations under healthcare rebate programs; Mallinckrodt's ability to navigate price fluctuations; future changes to U.S. and foreign tax laws; Mallinckrodt's ability to achieve expected benefits from restructuring activities; complex include autoimmune processes; competition; product liability losses and other litigation liability; ongoing governmental investigations; material health, safety and environmental liabilities; retention of key personnel; conducting business internationally; the effectiveness of information technology infrastructure; and cybersecurity and data leakage risks.

These and other factors are identified and described in more detail in the "Risk Factors" sections of Mallinckrodt's Annual Report on Form 10-K for the fiscal year ended September 30, 2016. 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

Investor Relations
Coleman N. Lannum, CFA
Senior Vice President, Investor Strategy & IRO
314-654-6649
cole.lannum@mallinckrodt.com

Daniel J. Speciale, CPA
Director, Investor Relations
314-654-3638
daniel.speciale@mallinckrodt.com

Media
Rhonda Sciarra
Senior Communications Manager
908-238-6765
rhonda.sciarra@mallinckrodt.com

Meredith Fischer
Chief Public Affairs Officer
314-654-3318
meredith.fischer@mallinckrodt.com

[1] American Heart Association Heart Disease and Stroke Statistics, 2013 update
[2] Callaway et al. Resuscitation. 2010 May; 81(5): 524–529.
[3] Merchant et al. Circulation: Cardiovascular Quality and Outcomes. 2009;2(5):421–428
[4] Accounting principles generally accepted in the U.S.

View original content with multimedia:http://www.prnewswire.com/news-releases/mallinckrodt-licenses-inhaled-xenon-gas-therapy-development-product-300528880.html

SOURCE Mallinckrodt plc

Print Page | RSS Feeds | Email Alerts

Building On Our Heritage
More than 150 years of quality, integrity and service.
Learn More

Our Culture
From philanthropic efforts to advocacy initiatives, we are living our values throughout our communities.
Learn How

Mallinckrodt, the 'M' brand mark, the Mallinckrodt Pharmaceuticals logo and other brands are trademarks of a Mallinckrodt company.™ 2018 Mallinckrodt. Mallinckrodt Pharmaceuticals is a registered business name of Mallinckrodt plc, which is registered in Ireland as a public limited company with registration number 522227 and has its registered office at College Business & Technology Park, Cruiserath, Blanchardstown, Dublin 15, Ireland.

Mallinckrodt uses cookies to improve and analyze site functionality. Some aspects of the site may not function properly without cookies enabled. To learn more about how we use cookies and how you can change your cookies settings, please read our Privacy Policy. By continuing to browse the site, you are agreeing to accept our use of cookies.

I Agree