



Chelsea Therapeutics CEO to Review NORTHERA(TM) NDA and Provide an Update on Upcoming Advisory Committee Meeting During Presentation at BIO CEO

Dr. Pedder's Presentation and Webcast is Scheduled for Today at 10:30 AM ET

CHARLOTTE, N.C., Feb. 13, 2012 (GLOBE NEWSWIRE) -- Chelsea Therapeutics International, Ltd. (Nasdaq:CHTP) announced that during a presentation at the 14th Annual BIO CEO and Investor Conference president and CEO, Dr. Simon Pedder, plans to provide an update regarding the company's New Drug Application (NDA) for NORTHERA™ (droxidopa), an overview of key issues identified in the FDA briefing document received by the company and anticipated discussion points for the upcoming Cardiovascular and Renal Drugs Advisory Committee (CRDAC) meeting scheduled for February 23rd.

FDA is currently reviewing Chelsea's application for marketing approval of Northera, an orally active synthetic precursor of norepinephrine, for the treatment of symptomatic neurogenic orthostatic hypotension (Neurogenic OH) in patients with primary autonomic failure (Parkinson's disease, multiple system atrophy and pure autonomic failure), dopamine beta hydroxylase deficiency and non-diabetic autonomic neuropathy. Under the Prescription Drug User Fee Act IV (PDUFA), FDA's goal is to review and act on the NDA by March 28, 2012.

"In light of recent communications with FDA, including receipt of a briefing document for our upcoming advisory committee meeting, we wanted to take this opportunity to update our shareholders on several lines of inquiry that have emerged as significant components of the benefit-risk analysis of Northera," commented Dr. Pedder. "A number of these questions relate to previously discussed issues identified for our development program, namely the short duration of our clinical studies, the limited size of our study population given the orphan indication and the challenges in quantifying symptomatic and clinical benefit. FDA has, however, placed increased emphasis on safety data from our long-term extension program and the post-marketing surveillance program in Japan. We look forward to the opportunity to address these questions in depth during the advisory committee meeting and to continuing to work with FDA to address any additional questions they may have regarding Northera and our clinical program."

During his presentation, Dr. Pedder plans to review key clinical portions of the Northera NDA filing, including combined safety and efficacy data from Chelsea's two completed Phase 3 efficacy studies in NOH (Studies 301 and 302), two long-term open-label extension studies, a dedicated thorough QTc study, and a 24-hour ambulatory blood pressure monitoring safety study.

Dr. Pedder also plans to provide an update on key issues identified in the FDA briefing document that Chelsea received in advance of the advisory committee meeting, including:

Clinical Endpoints in Neurogenic OH: The Orthostatic Hypotension Questionnaire Composite Score vs. The Orthostatic Hypotension Symptom Assessment Item #1 (Dizziness)

Neurogenic OH has historically been assessed on the basis of an improvement in standing systolic blood pressure (SBP). However, because the correlation between standing SBP and symptom relief has not been adequately demonstrated in any clinical trial, FDA advised us in 2007 that demonstrating improvement in standing SBP would not provide sufficient evidence of efficacy to support US marketing approval.

As a result, Chelsea assessed Northera's therapeutic effect using the orthostatic hypotension questionnaire (OHQ), the only validated patient reported outcome measure specifically designed to rate the severity of symptoms resulting from low blood pressure and the degree those symptoms interfere with a patient's ability to perform activities of daily living. Chelsea believes that demonstrating improvement on this questionnaire would permit a claim of symptomatic and functional improvement in patients with Neurogenic OH.

The OHQ is a two-part questionnaire that uses an 11-point scale (zero to 10) to assess the severity of six symptoms on the orthostatic hypotension symptom assessment scale (OHSAS) and four patient function criteria on the orthostatic hypotension daily activities scale (OHDAS). The composite OHQ score, the primary endpoint in Study 301, reflects the average improvement in mean OHSAS and OHDAS scores. As part of a global assessment of improvement, the OHQ specifically evaluates improvements in dizziness (OHSAS Item 1), widely thought to be the cardinal feature of Neurogenic OH.

Consistent with Chelsea's view in designing the Phase 3 studies, FDA's Study Endpoints and Labeling Development (SEALD) team determined that the concept of OHSAS Item 1 (dizziness, lightheadedness, feeling faint or "feeling like you might black out") was comprehensive unambiguous and consistent with core symptoms identified in the qualitative research and therefore has

content validity. By contrast, the same review determined that the scope of symptoms assessed by the OHSA is not fully aligned with symptoms discovered during qualitative research and that OHDAS questions should have specifically addressed patients' ability to make postural changes during their daily activities. Issues related to the validation of the OHQ are covered in depth in a recent publication "*The Orthostatic Hypotension Questionnaire (OHQ): validation of a novel symptom assessment scale*" published in *Clinical Autonomic Research* by Kaufman, et al. Nov 2011.

Given the robust outcome on both the OHQ composite and OHSA Item 1 in Study 301, Chelsea believes that any FDA questions regarding the suitability of outcome measures is likely to primarily be a factor in evaluating Study 302.

Duration of Clinical Trials: Long-term Efficacy and Safety

Study 301 demonstrated that Northera results in statistically significant symptomatic benefit as measured by the OHQ composite ($p=0.003$), OHSA Item 1 ($p < 0.001$), eight of the ten individual OHQ Item scores (all p less than or equal to 0.05) as well as standing systolic blood pressure ($p < 0.001$) for at least one week. Additionally, the results of Study 302 provide supportive evidence of the benefit of Northera as measured by the OHQ composite ($p=0.042$). However, Chelsea's Northera development program may not adequately establish a durable treatment effect as a result of the short duration of double-blind, placebo controlled clinical trials. Further, FDA is interested in the correlation between effect size and clinical benefit in this indication given the effect size of 0.9 and 1.3 on the OHQ composite and OHSA Item 1 in Study 301.

Turning to safety, Chelsea's Phase 3 efficacy studies are supported by two long-term, open-label safety studies (Study 303 and Study 304). As of the 90-day update, 658 patients had been treated with Northera for < 6 weeks, 281 for > 6 months, 167 for > 1 year and 28 for > 2 years, reflecting a large safety database for an orphan disease population. Over the course of Chelsea's long-term extension studies, 54 (17.9%) patients reported serious adverse events (SAEs), more than 85% of these SAEs were considered unlikely or not related to therapy. The most common SAEs (greater than or equal to 1% of patients) were syncope (2.3%), pneumonia (1.7%), sepsis (1%) and hip fracture (1.0%). This rate of SAEs is consistent with the overall study population that suffers from primary diagnosis frequently associated with a high rate of SAE and increased morbidity and mortality.

Over the course of Chelsea's development program, 19 patients died. Of these 19 patients, 1 died during screening prior to receiving drug, 1 patient died 11 days after discontinuing treatment and after resuming treatment with midodrine. A majority of the deaths, 11 of the 19, occurred in patients diagnosed with multiple system atrophy, a rapidly progressing disease in which the average life expectancy following positive diagnosis is approximately 7-9 years. Causes of death generally included sepsis, cardiopulmonary arrest, respiratory failure, pneumonia and pelvic fracture. All are considered common causes of death in this population. In total, only 3 deaths were noted by investigators as being possibly related to study drug. An independent clinical adjudication of all deaths requested by Chelsea concluded that the type and rate of deaths in the Northera program was similar to what would be expected in a similar cohort of patients with Neurogenic OH and didn't find meaningful evidence that treatment with Northera was causal in these deaths.

The FDA briefing document further notes the reports of neuroleptic malignant syndrome (NMS) from Japan. Neuroleptic malignant syndrome is a potentially life-threatening neurological disorder associated with drugs that affect the central dopaminergic system (including levodopa and dopamine agonists) and is most often caused by the rapid withdrawal or alteration of dopaminergic drugs in patients with Parkinson's disease. There have been no reported incidents of NMS in Chelsea's randomized controlled trials or long-term extension studies, nor is there any clear evidence that drugs acting on norepinephrine contribute to NMS.

Cardiovascular Safety Profile of Northera

Assessment of Northera's safety in this indication includes significant consideration of the cardiovascular profile including adverse events (AEs), serious adverse events (SAEs), and deaths considered to be cardiovascular in nature. The independent clinical adjudication of cardiovascular AEs and SAEs requested by Chelsea concluded that the adverse event rate seen in the Northera development program was similar to what would be expected in a similar cohort of patients with Neurogenic OH and didn't find meaningful evidence that treatment with Northera was causal in these adverse cardiovascular events.

FDA Briefing Document and Cardiovascular and Renal Drugs Advisory Committee

The CRDAC is an independent panel of experts that reviews and evaluates available data concerning the safety and effectiveness of products for use in the treatment of cardiovascular and renal disorders and makes recommendations regarding study design and product approvability to the FDA.

FDA intends to make background material available to the public no later than 2 business days before the meeting. Background materials, when available, or changes to the Advisory Committee meetings calendar can be found on the FDA website at <http://www.fda.gov/AdvisoryCommittees/Calendar/default.htm>.

FDA briefing documents for CRDAC contain the Review Division's assessments and/or conclusions prior to completion of the FDA review. Such assessments and conclusions do not necessarily represent the final position of the Review Division or Office.

Presentation at 14th Annual BIO CEO & Investor Conference

Dr. Simon Pedder is scheduled to present at the 14th Annual BIO CEO & Investor Conference at 10:30 AM ET on Monday, February 13th at the Waldorf Astoria Hotel in New York City.

Dr. Pedder's presentation will be webcast live and archived for 90 days on Chelsea's website, www.chelseatherapeutics.com.

About NORTHERA™ (droxidopa)

NORTHERA™ (droxidopa), the lead investigational agent in Chelsea Therapeutics' pipeline, has been studied in two Phase 3 clinical trials for the treatment of symptomatic neurogenic orthostatic hypotension (Neurogenic OH) in patients with primary autonomic failure -- a group of diseases that includes Parkinson's disease, multiple system atrophy (MSA) and pure autonomic failure (PAF). Droxidopa is a synthetic catecholamine that is directly converted to norepinephrine (NE) via decarboxylation, resulting in increased levels of NE in the nervous system, both centrally and peripherally. Droxidopa previously demonstrated clinical benefits in treating intradialytic hypotension, fibromyalgia and adult attention deficit hyperactivity disorder in Phase II trials.

About Chelsea Therapeutics

Chelsea Therapeutics (Nasdaq:CHTP) is a biopharmaceutical development company that acquires and develops innovative products for the treatment of a variety of human diseases, including central nervous system, rheumatoid arthritis, psoriasis and other inflammatory diseases. Founded in 2004 around its library of unique anti-inflammatory and autoimmune technology, Chelsea has further expanded its product development portfolio with early- and late-stage candidates that leverage the company's development expertise and accelerate the company's drug commercialization efforts. For more information about the company, visit www.chelseatherapeutics.com.

This press release contains forward-looking statements regarding future events. These statements are just predictions and are subject to risks and uncertainties that could cause the actual events or results to differ materially. These risks and uncertainties include risk of regulatory approvals; risks and costs of drug development, including the uncertainty of cost, timing and outcome of clinical trials; our need to raise operating capital; our reliance on our lead drug candidates droxidopa and CH-4051; our history of losses; reliance on collaborations and licenses; intellectual property risks; competition; market acceptance for our products, if any are approved for marketing; and reliance on key personnel including specifically Dr. Pedder.

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