

November 17, 2017

Healthcare

Industry Update

Key Takeaways – The Impact of The Opioid Epidemic on The Pain Management Landscape

- **Conclusions** – We hosted a key opinion leader luncheon with three physician experts in the field Joseph Pergolizzi, M.D., Chris Gharibo, M.D., and R. Norman Harden, M.D. discussing the impact of the opioid epidemic on the pain management landscape. They believed pain is not being treated optimally, with wax and wane phases in the use of pain medication. Patients were either overtreated with indiscriminate prescription of opioids in the past two decades or being under treated in the recent times. They highlighted the need for optimization of pain medication use and tailoring pain treatments for each of the patients based on their pain pathophysiology.
- **Pain research still in infancy** – There has been focus on pain research only in the past forty years despite pain being a widely prevalent condition. There are still limited options for pain treatment and no reliable biomarkers for pain. There is a significant amount research needed to understand multifactorial etiology of pain and develop treatments.
- **Targeted approaches expected to produce results** – The experts believe that while broad spectrum approaches like opioids have a place in the treatment of pain, more targeted approaches focusing on the etiology of pain have better potential to produce optimal results of better pain management without challenges associated with broad spectrum approach. Continuous infusions of NSAIDs expected to reduce analgesic gap.
- **Need for innovative drugs** – The experts believe that most of the pain drugs are repurposed and there is a need for innovative multi mechanistic drugs which can target high co-morbidities like anxiety, depression, sleep disorders and psycho-social issues.
- **Focus on clinically meaningful outcomes** – Drug developers should focus on treating chronic pain to increase functionality, activities of daily living, and quality of life. They also expect payor and regulator focus on pharmaco-economic outcomes.

Equity Research

Kumaraguru Raja, PhD, Director, Senior Biotechnology Analyst
(646) 462-4671 kumar.raja@brooklinecm.com

Brookline Capital Markets

Trading: (646) 807-4124 Institutional Sales: (646) 807-4125
www.Brooklinecapitalmarkets.com

Refer to Page 4 for Analyst Certification & Disclosures

Key Takeaways – The Impact of The Opioid Epidemic on The Pain Management Landscape | November 17, 2017**Key Takeaways – The Impact of The Opioid Epidemic on The Pain Management Landscape**

The experts, Joseph Pergolizzi, M.D., Chief Operating Officer of NEMA Research Inc in Naples, Florida and Chairman of the Abstract and Poster Selection Committee for PAIN Week, and a member of the CHANGE PAIN Board, Chris Gharibo, M.D., an Associate Professor of Anesthesiology at NYU Langone Medical Center, and the Medical Director of Pain Medicine, at NYU Langone's Hospital for Joint Diseases, and R. Norman Harden, M.D., Professor Emeritus in the departments of Physical Medicine and Rehabilitation and Physical Therapy and Human Movement Sciences at Northwestern University, believed that pain is not optimally treated and there is need for moderation in the use of pain medications with treatments tailored to pathophysiology. There are no biomarkers for pain, which complicates the treatment as well as development of new drugs for pain. The Global Pain Initiative working on facial recognition and other modalities to quantify pain. Most pain drugs are repurposed, not a lot of innovative drugs approved and there is a desperate need for innovation and creativity in the space as significant unmet need remains. Patients treated for pain have high co-morbidities with anxiety, depression and psycho-social issues, which also need to be addressed.

New Drugs Should Focus on Clinically Meaningful Outcomes

New pain drugs should lead to meaningful improvements, need to be balanced with side effects and designed such that patients can be compliant with treatment. In treating chronic pain, the main goal is to increase functionality, activities of daily living, and quality of life. Drug developers should focus on clinically meaningful end points and potentially conduct clinical trials with active comparators. They believe that pharmaco-economics as an outcome will be the focus of regulators and payors. One of the experts believed that while multidisciplinary models of pain management seem promising in theory, they are not preferred by patients and payors. While drug developers are trying to mitigate regulatory risk by using FDA accepted endpoints, they should also focus on health economics and outcomes research as intrinsic value is needed for payor reimbursement.

Key Takeaways – The Impact of The Opioid Epidemic on The Pain Management Landscape | November 17, 2017

Regulators like the FDA want drugs to be tested on heterogenous models like diabetic nephropathy which includes multiple pathophysiology's and it may be difficult to develop pain medication due to heterogenous nature of these population. Pain drugs are expected to improve other aspects of pain management such as function.

Continuous Infusions of NSAIDS Expected to Reduce Analgesic Gap

Nonsteroidal Anti-inflammatory Drugs (NSAIDs) dosing and exposure level based on pharmacodynamics is too high, which leads to the side-effect profile. Tissue kinetics, based on how quickly and effectively NSAIDs can get into tissue impact the analgesic effect. Focus is shifting to NSAID sparing models to mitigate the side effect profile. Lower dose of continuous infusions of NSAIDs are expected to overcome the challenge of analgesic ceiling effect and reduce analgesic gap.

Need for non-NSAID and non-opioid Drugs

The experts believe that there is a need for non-NSAID and non-opioid drugs. The experts believe that antibodies against nerve growth factor (NGF), sodium channel blockers, microglia system agonist need to watch as they could have potential in pain. They expect challenges for pain drugs targeting cannabinoid receptors as more state legalize medicinal, and recreational cannabinoids. One of experts believed targeting the ion channel receptor physiology is wide open as multiple ion channels play a role in pain pathophysiology. One of the experts believed bisphosphonates should still be considered investigational for Complex regional pain syndrome (CRPS) as a lot of data is not available, but should be considered as an option. While Ketamine in being used in post-operative settings, there is a need for better formulations. The experts believe that radiopharmaceuticals like Strontium chloride, which can be used in the palliative treatment of pain associated with metastatic bone disease, will have uptake if physicians are educated on its benefits.

Important Disclosures and Disclaimers

Distribution:

This report and all information contained within is intended for qualified institutional or professional clients of Brookline Capital Markets and qualified prospective institutional clients and is not meant for redistribution. The contents of this report represent the views, opinions, and analyses of its author. The information contained herein does not constitute financial, legal, tax or any other advice. All third party data presented herein were obtained from publicly available sources which are believed to be reliable; however, Brookline makes no warranty, express or implied, concerning the accuracy or completeness of such information. In no event shall Brookline be responsible or liable for the correctness of, or update to, any such material or for any damage or lost opportunities resulting from use of this data.

Analyst Certification:

I, Kumaraguru Raja, hereby certify that the views expressed in the foregoing research report accurately reflect my personal views about the subject securities and issuer(s) as of the date of this report. I further certify that my compensation is not directly, or indirectly, related to the specific recommendations or views contained in this report.

Financial Interests:

The analyst, Kumaraguru Raja, has no financial interest in the debt or equity securities of the subject company of this report. Further, no member of his household has any financial interest in the securities of the subject company. Neither the analyst, nor any member of his household is an officer, director, or advisory board member of the issuer(s) or has another significant affiliation with the issuer(s) that is the subject of this research report. The analyst has not received compensation from the subject company. At the time of this research report, the analyst does not know or have reason to know of any other material conflict of interest.

Brookline Capital Markets

Brookline Capital Markets is a division of CIM Securities, LLC. Brookline Capital Markets is a member of FINRA and SIPC. Brookline does not make a market in the securities mentioned in this report, and does not have an ownership interest in the securities. Brookline intends to solicit investment banking business from the subject company in the next three months. Brookline has not managed or co-managed a public offering for the subject company, nor received compensation for investment banking activity from the subject company in the 12 months prior to publication.

Definitions of ratings:

Key Takeaways – The Impact of The Opioid Epidemic on The Pain Management Landscape | November 17, 2017

Buy: Potential returns of more than 15% above current market price

Hold: Potential for the securities to decline or appreciate less than 15%

Sell: Potential for the securities to decline more than 15% from current market price

Total companies covered: 3. % of Buy recommendations: 100. % of Hold recommendations: 0. % of Sell recommendations: 0.