Press Release **For Immediate Dissemination**

Glenmark's novel molecule 'GRC 17536' for pain and respiratory conditions successfully completes Phase I trials in Europe

- GRC 17536 targeting TRPA1 receptor is a potential first-in-class molecule globally
- Glenmark plans to initiate Phase IIa studies and has completed regulatory submissions with MHRA, UK and BfArM, Germany for diabetic painful neuropathy
- The TRP family of ion channels have generated lot of interest globally due to their distinguishing role in pain signal transmission
- With this announcement, Glenmark has reaffirmed its position globally as a leader in the TRP space

February 14, 2012: Glenmark Pharmaceuticals today announced that its Novel Chemical Entity(NCE) 'GRC 17536' has completed Phase I trials (Single Ascending dose and Multiple Ascending dose) in the Netherlands. GRC 17536 is a global first-in-class program targeting the TRPA1 receptor antagonists for pain and respiratory disorders. TRPA1 belongs to Transient Receptor Potential (TRP) family of ion channels, which have generated a lot of interest as pain targets due to their distinguishing role in peripheral and/or central pain signal transmission.

In the Phase I trials for both the single ascending dose and multiple ascending dose, the drug was well tolerated up to the maximum dose tested. In addition, a good pharmacokinetic profile has been observed with no apparent gender or age effect. The overall exposures achieved in humans compares favorably with the exposure required for maximum efficacy in the animal models, which suits entry into further clinical development.

Glenmark has now planned to initiate Phase II studies in Pain indications. The company has filed regulatory submissions with the MHRA, UK, and BfArM, Germany, to initiate Phase 2a proof-of-concept study in patients with painful diabetic peripheral neuropathy. This double-blind, parallel group, placebo controlled study is designed to provide efficacy endpoints upon several weeks of dosing. Subject to regulatory approvals, the projected start of the study is March 2012.

Additionally, GRC 17536 will be tested via the inhaled route for use in the respiratory indications. Good efficacy has been observed for GRC 17536 when administered via inhaled route in preclinical pharmacology studies. Phase 1 enabling toxicity studies via inhalation route for GRC 17536 are nearing completion. Glenmark aims to initiate human inhalation studies by June 2012 with an integrated Phase 1/2a protocol in healthy adult volunteers and mild asthmatics followed by an allergen challenge study in patients with mild asthma.

Glenn Saldanha, Chairman & MD, Glenmark Pharmaceuticals ltd mentioned "This is a significant milestone for us and we are excited that our TRPA1 discovery program moving ahead in clinical development. This is another potential first-in-class molecule indicated for both pain and respiratory conditions. There is a huge unmet medical need in both therapeutic areas globally."

Glenmark is now positioned as one of the leading companies engaged in the discovery of novel TRP antagonists. Previously Glenmark has worked on TRPV1 and TRPV3 receptors and was able to successfully bring programs into clinical development. Both of these programs also resulted in out-licensing deals for Glenmark. To date, Glenmark has discovered several distinct scaffolds of highly potent TRPA1 antagonists with drug-like properties and has filed patent applications for these molecules.

GRC 17536, which is Glenmark's lead, is a highly potent (< 10nM) TRPA1 antagonist, which is highly selective (> 1000 fold over other TRPs). It has proven highly efficacious in treating inflammatory and neuropathic pain in animal models compared to gold standard drugs. It reversed hyperalgesia in in-vivo models of Freund's complete adjuvant – induced inflammatory and chronic constriction injury (CCI) – induced neuropathic pain with an EC50 of less than 10 mg/kg. In addition, when tested in an in-vivo model of asthma, it showed promising effect on airway inflammation, bronchoconstriction and cough. In the Phase 1 enabling GLP studies, the compound has showed good safety in the genotoxicity, safety pharmacology and toxicology studies.

Note on TRPA1

Over the last decade, a lot of interest has been generated in transient receptor potential (TRPs) channels as pain targets due to their distinguishing role in peripheral and/or central pain signal transmission. The transient receptor potential ankyrin 1 (TRPA1) receptor is implicated in miscellaneous pathologies including noxious cold, chemical and mechanical induced pain and hyperalgesia conditions. TRPA1 gene knock-out studies resulted in impaired sensory function to noxious cold, chemical and mechanical stimuli, suggesting that TRPA1 represents an important target for development of therapeutics for inflammatory and neuropathic pain conditions. In animal studies, activation of TRPA1 by the noxious agents causes pain and neurogenic inflammation, which could be blocked by treatment with TRPA1 antagonists or gene-specific antisense oligonucleotides. Recently, TRPA1 receptor has been shown to mediate responses to major ingredients from cigarette smoke namely H2O2 and crotonaldehyde. Oxidant activation of airway neurons is known to induce respiratory depression, nasal obstruction, sneezing, cough, and pain and it is observed that all these responses are absent in TRPA1 deficient mice. These two observations suggest TRPA1 functional blockade as a promising approach in treating airway hyper-reactivity during asthma/COPD.

Addressable market

The addressable market for Asthma/COPD is approx USD 30 billion while the addressable market for osteoarthritis and neuropathic pain in approx USD 10 billion. There is a huge unmet medical need in both therapeutic areas.

About Glenmark Pharmaceuticals Ltd

Glenmark Pharmaceuticals Ltd. (GPL) is a research-driven, global, integrated pharmaceutical company headquartered at Mumbai, India. It is a leading player in the discovery of new molecules both NCEs (new chemical entity) and NBEs (new biological entity). Glenmark has six molecules in various stages of clinical development and is primarily focused in the areas of Inflammation [asthma/COPD, rheumatoid arthritis etc.] and Pain [neuropathic pain and inflammatory pain]. The company has a significant presence in branded generics markets across emerging economies including India. GPL along with its subsidiary has twelve manufacturing facilities in four countries and has five R&D centres.

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