

**Press Release****For Immediate Dissemination**

## **Glenmark's novel molecule 'GRC 27864' for chronic inflammatory diseases including pain entering human trials**

- GRC 27864 is a potent, selective, orally bioavailable inhibitor of mPGES-1
- The molecule has successfully completed pre-clinical and Phase 1 enabling studies. Regulatory submission has been filed for Phase 1 trial (first-in-human) with MHRA, UK
- mPGES-1 inhibitors selectively block the production of PGE<sub>2</sub> while sparing other prostanoids of physiological importance
- With this announcement, Glenmark has reaffirmed its position globally in the development of novel pain therapies

**Mumbai, India April 3, 2014:** Glenmark Pharmaceuticals today announced that its Novel Chemical Entity (NCE) 'GRC 27864' is entering human trials. This NCE program targets Microsomal Prostaglandin E synthase-1 (mPGES-1) as a novel therapeutic target in pain management. Selective mPGES-1 inhibitors are expected to inhibit increased prostaglandin E2 (PGE<sub>2</sub>) production in the disease state without affecting other prostanoid metabolites and, consequently, may be devoid of the GI (gastrointestinal) and cardiovascular side effects seen with NSAIDs and COX-2 inhibitors, respectively.

Glenmark has completed preclinical studies and Phase 1 enabling GLP studies for its selected lead molecule, GRC 27864 and has filed a Phase 1 application for first-in-human trial with the MHRA, UK. The Phase 1 studies are to be initiated soon and are likely to get completed by January 2015. Following this, Glenmark will also be initiating a proof of concept study in patients with acute pain.

**Dr. Michael Buschle, Chief Scientific Officer, Glenmark Pharmaceuticals Ltd., mentioned** "We are excited that our mPGES-1 discovery program is moving forward to human trials. This is another potential first-in-class molecule and there is a significant unmet medical need. This announcement also reaffirms our position globally in the development of novel pain therapies"

GRC 27864 is a potent, selective, and orally bioavailable inhibitor of mPGES-1, an enzyme which is up-regulated under inflammatory conditions. Blocking the mPGES-1 enzyme is a novel strategy and expected to selectively inhibit increased PGE<sub>2</sub> production during inflammation, without affecting other prostanoids of physiological importance. PGE<sub>2</sub> is a potent pro-inflammatory prostanoid and mediator of inflammatory response, which has been implicated in many pathological conditions including inflammation, pain, atherosclerosis, and fever. Thus, GRC 27864 has the potential to be beneficial in the chronic treatment of inflammatory diseases and associated pain.

GRC 27864 is currently being developed as a drug for the potential treatment of chronic inflammatory disorders such as osteoarthritis (OA) and rheumatoid arthritis (RA).

**Note on mPGES-1**

PGE<sub>2</sub> is a lipid mediator produced by arachidonic acid, which serves pivotal functions in disease conditions associated with fever, inflammation, and pain. mPGES-1 is a terminal enzyme in the PGE<sub>2</sub> biosynthetic pathway and solely responsible for PGE<sub>2</sub> synthesis during inflammation. Over expression of mPGES-1 is observed in various nonclinical animal models, such as RA, OA, atherosclerosis, experimental autoimmune encephalomyelitis, cancer, inflammatory bowel disease, multiple sclerosis, periodontitis, fibrosis, Parkinson's disease, and Alzheimer's disease. On the contrary, mPGES-1 deleted cells produced significantly lower levels of PGE<sub>2</sub> in response to inflammatory stimuli and were less sensitive to inflammatory and neuropathic pain, and refractory to the development of joint pathology in rodent arthritis models. Selective mPGES-1 inhibitors are expected to inhibit increased PGE<sub>2</sub> production in the disease state without affecting other prostanoid metabolites and are, consequently, may be devoid of the GI and cardiovascular side effects seen with NSAIDs and COX-2 inhibitors, respectively, potentially making them suitable for chronic treatment of inflammatory diseases that are accompanied with pain.

**Addressable market**

Recent reports indicate that more than 1.5 billion people worldwide suffer from chronic pain in some form with a direct correlation between incidence rates and increasing age. It is estimated that, at some point in their lives, 20% of the global adult population suffers from pain with 10% of newly diagnosed cases of chronic pain being added each year. Despite incremental advances in opioid-based or cyclooxygenase-based therapies, there has been little success in identifying and developing treatments based upon new targets that might overcome the limitations of currently available analgesic treatments for the management of chronic pain.

**About collaboration with Forest**

Glenmark has entered into a Collaboration and Option Agreement with Forest Laboratories ("Forest"), a leading, fully integrated, specialty pharmaceutical company, for the development of novel mPGES-1 inhibitors to treat chronic inflammatory conditions, including pain. Forest has an exclusive option to obtain license rights to the program upon the completion of Phase 1 clinical trials. Under the terms of the agreement signed in FY 2013, Forest made USD 6 million upfront payment and also provided an additional USD 3 million to support the next phase of work. In September 2013 and March 2014, Glenmark received additional amounts of USD 2 million and USD 4 million, respectively, as research fee payments from Forest. Hence, the total amount received by Glenmark from Forest towards its novel mPGES-1 inhibitors program is USD15 million.

**About Glenmark Pharmaceuticals Ltd**

Glenmark Pharmaceuticals Ltd. (GPL) is a research-driven, global, integrated pharmaceutical company and ranked among the top 80 Pharma & Biotech companies of the world in terms of revenues. Glenmark is a leading player in the discovery of new molecules both NCEs and NBEs. Glenmark has several molecules in various stages of clinical development and primarily focused in the areas of Inflammation, Pain and Oncology. The company has significant presence in branded formulations across emerging economies including India. Its subsidiary, Glenmark Generics Limited services the requirements of the US and Western Europe markets.

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