

# ROPINIROLE (REQUIP) NON-CONFIDENTIAL DISCLOSURE

## I. HISTORY AND BACKGROUND

- Ropinirole (4-[2-(dipropylamino)-ethyl]-1,3-dihydro-2H-indol-2-one) is a second-generation dopamine 2/3 receptor agonist. It was developed by GlaxoSmithKline (GSK), and FDA approved for treatment of Parkinson's disease (PD) in 1997 and for restless legs syndrome (RLS) in 2005.
- Because of its benefit for RLS and the association of RLS with fibromyalgia (FM), dopamine agonists are considered a new treatment option for FM, a condition affecting 6-12 million Americans without an FDA approved treatment.

## II. PROFILE OF ROPINIROLE

- **Neurochemistry.** Ropinirole has greater affinity for D<sub>3</sub> compared to D<sub>2</sub> and D<sub>4</sub> receptors without significant affinity for D<sub>1</sub>, D<sub>5</sub>, serotonin, acetylcholine, histamine, GABA, muscarinic, opioid,  $\alpha_1$ -adrenergic,  $\alpha_2$ -adrenergic or  $\beta$ -adrenergic receptors. Its beneficial effect in FM is thought to be the result of enhanced D<sub>3</sub> mediated hippocampal dampening of autonomically induced fragmentation of stage IV, non-REM sleep.<sup>1</sup>
- **Fibromyalgia:** Investigational treatment of FM with ropinirole was first reported in 2003<sup>2</sup> in the *Journal of Clinical Rheumatology*, and a pilot, randomized, placebo-controlled trial was reported at the annual meetings of the American College of Rheumatology<sup>3</sup> and British Society for Rheumatology in 2004. In 30 patients, 45% of active subjects (20) noted >50% reduced FM pain, while 30% of those receiving placebo (10) noted >50% reduced pain. Although not statistically significant due to small sample size, all other secondary outcome measures favored ropinirole, including improved fatigue, function and global assessments.
- **Safety.** Extensive published reports in clinical trials with ropinirole indicate that it is well tolerated even in a high-risk elderly population with PD. In the FM trial, the primary adverse event was mild, transient nausea.

## III. PATENT STATUS

- A patent describing this method of treating FM with ropinirole has been granted to Andrew J. Holman, MD in the US (2001), South Africa (2004), Singapore (2005), and Mexico (2005). Additional international applications are pending.
- GSK holds the compound patent for ropinirole, which will expire in 2006.

## IV. LICENSING STRATEGY.

Inmedix seeks a partner to develop, market, and sell ropinirole on a worldwide basis for treatment of FM.

## V. Additional materials are available upon request. Please contact Tim Sciarrillo, CEO at [tim@inmedix.com](mailto:tim@inmedix.com) or 1-800-775-4902

1. Wood PB. Fibromyalgia syndrome: a central role for the hippocampus- a theoretical construct. *J Musculoskeletal Pain* 2004;12(1):19-26.

2. Holman AJ. Ropinirole, a dopamine agonist, for refractory fibromyalgia: preliminary observations. [letter] *J Clin Rheum* 2003;9(4):277-9.

3. Holman AJ. Treatment of fibromyalgia with the dopamine agonist ropinirole: a 14-week double-blind, pilot, randomized controlled trial with 14-week blinded extension. *Arthritis Rheum* 2004;50(9)suppl; A1870.