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PRESS RELEASE

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**ROTTAPHARM ANNOUNCES FAVOURABLE RESULTS OF A PIVOTAL PHASE III
TRIAL OF DEXLOXIGLUMIDE IN IRRITABLE BOWEL SYNDROME (IBS)**

Milan, May 17, 2007 – Rottapharm, an Italian pharmaceutical company, announced today that it has obtained favourable topline results in a pivotal phase III trial of dexloxyglumide in patients with constipation – predominant Irritable Bowel Syndrome (C-IBS). These topline results relate to the analysis of the primary efficacy outcome of the DARWIN trial (“Dexloxyglumide, A Randomization/Withdrawal IBS Novel” trial).

The study was performed according to a randomised discontinuation study design, in which over 400 patients with C-IBS who were “responders” to an 8 to 12-week treatment course with dexloxyglumide, were randomised to continue with either dexloxyglumide or with placebo over an additional 24 weeks, in a double-blind fashion. At the end of the 24-week randomized, double-blind period, there was a highly significant 16.2% difference in maintenance of the responder status in dexloxyglumide-treated patients compared to those who received placebo. The time-to-relapse analysis by the Log Rank Test over the 6 months of treatment provided $P=0.001$ in favour of dexloxyglumide. The responder status was assessed on the basis of a combination endpoint consisting of the standard Subject Global Assessment (SGA), which is a validated outcome that captures the patient overall evaluation of IBS symptoms, and the patient assessment of abdominal pain control, with a correction for the possible use of rescue laxatives.

These results were seen in the primary efficacy population, which was restricted to females with C-IBS. A separate analysis in a smaller stratified subset of male patients did not show any difference between dexloxyglumide and placebo, thus being consistent with



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previous results with other experimental drugs for IBS whose efficacy seemed to be restricted to the female gender only.

Dexloxiplumide is a cholecystokinin-1 (CCK-1) receptor antagonist, that affects both gastro-intestinal motility and visceral sensory pathways. Following promising results in a Phase II program conducted in UK by Rottapharm, two phase III clinical trials performed in the US in collaboration with Forest Laboratories, Inc. (Rottapharm license partner for the US territory), failed to show a significant difference between dexloxiplumide and placebo, despite a numeric trend in favour of the former in both studies. However, these two previous trials were conducted according to the FDA recommendations for trials of 12-week duration in IBS. Conversely, the EMEA recommends that trials of novel IBS drugs assess their efficacy either over repeated shorter term-cycles, or as a long-term (≥ 6 months) maintenance treatment.

“In discussions with the European agency”, explains Prof. Lucio Rovati, Chief Scientific Officer of Rottapharm, “we realized that they were not comfortable with a 12-week treatment duration, which was then confirmed in the agency guidelines for IBS drugs, and we agreed to perform a long-term maintenance study in Europe. The DARWIN trial allowed us to implement such an objective according to a novel study design, the randomization/withdrawal, that has attracted a lot of interest within the scientific community and regulatory agencies, including the FDA”.

Dexloxiplumide, if approved, would be the first of a new class of drugs for IBS, a high-prevalence indication that experienced the withdrawal from the market of serotonin receptor modulators, alosetron (Glaxo; for diarrhea-predominant IBS) and recently tegaserod (Novartis; for constipation-predominant IBS), for safety reasons.

Safety was good in the DARWIN trial, similar to what has been observed in the overall phase II and phase III program. This program has so far included over 1000 patients receiving placebo and over 2500 patients treated with dexloxiplumide in studies with durations of exposure between 12 and over 52 weeks.



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Once all ancillary analyses have been completed, the DARWIN trial data will be presented to the regulatory agencies to get advice on further steps for the IBS indication.

In the meantime, clinical studies in other functional gastro-intestinal disorders are ongoing.

About Rottapharm

Rottapharm is a multinational pharmaceutical group based in Italy. The Group was founded in 1961 as Rotta Research Laboratorium, an independent research laboratory which is now the headquarters of the group renamed Rottapharm S.p.A. The mission of Rottapharm is the discovery, development and distribution around the world of new original drugs. Rottapharm's strategic therapeutic areas are osteoarticular, gynaecology, dermatology, cardiovascular and gastroenterology. Moreover, in recent years, targeted company acquisitions allowed Rottapharm to reach a leading position in the personal care pharmacy market in Europe. A state-of-the-art nutraceutical research and marketing segment has also been implemented.

Rottapharm has arrangements in progress for the development of eleven new chemical entity projects deriving from its own internal discovery. These projects involve compounds directed to rheumatic, gastroenterological, respiratory, CNS and oncological disorders. Arrangements include development through Rottapharm's own internal capabilities for most of the compounds and co-development with industrial partners for some of them.



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