

March 19, 2015

Opicapone significantly improves OFF-time in fluctuating Parkinson's Disease patients as add-on to levodopa

PORTO, PORTUGAL, Thursday 19 March 2015 – BIAL announced results from a Phase III, randomized, double-blind, active- and placebo-controlled, parallel group study (BIPARK-I) evaluating opicapone (BIA 9-1067), a novel once-daily catechol-O-methyltransferase (COMT) inhibitor for use as adjunctive therapy in levodopa-treated Parkinson's disease patients. In the study, opicapone 50 mg once-daily achieved significant reductions in absolute "wearing-off"-time in Parkinson's disease. Significant improvements were also observed in Investigators' and Subjects' Global Assessment of Change. The improvement tendency was significant compared to placebo and also entacapone, respectively. Opicapone was considered overall safe and well tolerated.

Attached from the following page is the press release made by BIAL for your information.

In April 2013, ONO PHARMACEUTICAL CO.,LTD. (Osaka, Japan, President and Representative Director:Gyo Sagara) entered into a license agreement with BIAL to exclusively develop and commercialize opicapone (ONO-2370) in Japan, and the Phase I clinical study is being conducted. Outside Japan, BIAL is conducting the Phase III clinical studies. Opicapone shows a long-lasting effect on COMT inhibition from once daily dosing in clinical studies so far, and is expected to improve patient outcomes and offer dosing convenience compared to the existing COMT inhibitor.

Contact

ONO PHARMACEUTICAL CO., LTD.

Corporate Communications

public_relations@ono.co.jp

Opicapone significantly improves OFF-time in fluctuating Parkinson's Disease patients as add-on to levodopa

- **BIAL releases data from the BIPARK-I phase 3 pivotal study**
- **Patients taking opicapone 50 mg once-daily had 2 hours less absolute OFF-time**
- **Data presented at the 12th International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PD™ 2015)**

FOR IMMEDIATE RELEASE

PORTO, PORTUGAL, Thursday 19 March 2015 – BIAL today announced results from a Phase 3, randomized, double-blind, active- and placebo-controlled, parallel group study (BIPARK-I) evaluating opicapone (BIA 9-1067), a novel once-daily catechol-O-methyltransferase (COMT) inhibitor for use as adjunctive therapy in levodopa-treated Parkinson's disease patients. In the study, opicapone 50 mg once-daily achieved significant reductions (2.0 hours) in absolute OFF-time ($p=0.0005$ vs 0.9 hours for placebo). Significant improvements were also observed in Investigators' and Subjects' Global Assessment of Change. The improvement tendency was significant compared to placebo ($p=0.0005$, $p=0.0008$) and also entacapone ($p=0.007$, $p=0.0091$), respectively. Opicapone was considered overall safe and well tolerated.

Detailed study results will be presented today during a poster session at the 12th International Conference on Alzheimer's and Parkinson's Diseases and Related Neurological Disorders (AD/PD™ 2015) in Nice, France (Abstract 5-1075).

Professor Joaquim Ferreira, Professor of Neurology and Clinical Pharmacology at the University of Lisbon, said, "In the last 10 years, there have been few new treatment options in Parkinson's disease. Opicapone intends to fulfil the need for a more potent COMT inhibitor."

Professor Andrew Lees, Professor of Neurology at the National Hospital for Neurology and Neurosurgery, London, added, "Opicapone offers an important alternative to the currently available COMT inhibitors, with convenient once-daily dosing."

The continued development of opicapone reflects BIAL's commitment to discover, develop and provide new therapeutic solutions to patients. According to António Portela, CEO of BIAL, "Opicapone provides new hope for clinicians and patients. We are proud of the long-term strategy we've implemented focused on Research and Development and of the therapeutic innovation programme that has developed this therapy."

BIAL is an international pharmaceutical group with products available in more than 50 countries.

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About opicapone

Opicapone once-daily is a novel catechol-O-methyltransferase (COMT) inhibitor, providing potent and sustained COMT inhibition. This action enhances the beneficial effects of levodopa in Parkinson's disease patients with motor fluctuations.

Opicapone is supported by a large and comprehensive clinical development programme. BIPARK-I is the second of two Phase 3 double-blind, randomized, parallel-group, multicenter clinical studies to report results from the double-blind phase. Open-label phases of both studies are due to report in 2015.

The opicapone EU marketing authorization application has been successfully validated and is now under review by the European Medicines Agency (EMA).

About the BIPARK I study

BIPARK-I is a Phase 3, randomized, double-blind, active- and placebo-controlled, parallel group efficacy and safety study in levodopa-treated patients with idiopathic Parkinson's disease and motor fluctuations.

The efficacy and safety of three different doses (5, 25 and 50 mg) of opicapone administered once-daily, compared with entacapone (200 mg) or placebo administered with each dose of levodopa, were assessed. Opicapone 50 mg once-daily successfully achieved superiority compared to placebo and non-inferiority against entacapone.

The study enrolled 600 patients from 106 study sites in Europe. Patients were 34-83 years-old and had a diagnosis of idiopathic Parkinson's disease for at least 3 years; had a modified Hoehn & Yahr Scale stage of ≤ 3 in the ON state; had to receive optimum levodopa therapy (3-8 daily doses), stable for at least 4 weeks; had signs of end-of-dose deterioration (wearing-OFF) for at least 4 weeks with a mean daily OFF-time of 1.5 hours while awake, not including morning pre-first dose OFF-time; and had the ability to keep accurate 24-hour diaries. Patients were randomly assigned in a 1:1:1:1:1 ratio to opicapone 5 mg, 25 mg or 50 mg, entacapone and placebo.

The primary endpoint was the mean change from baseline in absolute OFF-time, as measured by 24-hour diaries. Secondary endpoints included proportion of responders, and Investigators' and Subjects' Global Assessment of Change, tolerability and safety assessments.

About Parkinson's disease

Parkinson's disease is a degenerative disorder of the central nervous system characterized by bradykinesia (slowness of movement), tremor, muscle rigidity and postural instability.

The clinical manifestations usually start after the age of 50 years (average age for diagnosis is approximately 60 years) and the incidence increases with age. The prevalence is estimated at 300 per 100,000 inhabitants, increasing to 1/100 over the age of 55-60 years.

Therapeutic strategies are available to improve the signs and symptoms of the disease.

About BIAL

Founded in 1924, BIAL's mission is to discover, develop and provide therapeutic solutions within the area of health. In recent decades, BIAL has focused on quality, innovation and internationalization.

It is the partner of choice for many companies, having a strong presence in the Iberian Peninsula as well as in over 10 countries in Latin America and in several French- or Portuguese-speaking African countries.

BIAL is strongly committed to therapeutic innovation, investing more than 20% of its turnover in research and development (R&D) every year, placing it among the most innovative European companies. Key research areas for BIAL are the central nervous system, the cardiovascular system and allergen immunotherapy.

BIAL's innovative programmes focus on continuing the clinical development of its anti-epileptic Zebinix/Aptiom (on the market in Europe and the USA), as well as opicapone for Parkinson's disease.

With a team of 900 employees, BIAL has reinforced its international presence, an aspect that the company will strengthen over the next decade.

Further information about BIAL can be found at www.bial.com.

Contact:

Susana Vasconcelos

BIAL

susana.vasconcelos@bial.com

Lydia Jenkins

iS Health

lydia@is-health.co.uk

+44 1252 733353