## Press Release

# Impax Pharmaceuticals Announce FDA Approval of RYTARY™ (Carbidopa and Levodopa) Extended-Release Capsules for the Treatment of Parkinson's disease

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HAYWARD, Calif., Jan. 8, 2015 /PRNewswire/ -- Impax Pharmaceuticals, a division of Impax Laboratories, Inc. (NASDAQ: IPXL), today announced that the U.S. Food and Drug Administration (FDA) approved RYTARY, an extended-release oral capsule formulation of carbidopa-levodopa, for the treatment of Parkinson's disease, post-encephalitic parkinsonism, and parkinsonism that may follow carbon monoxide intoxication and / or manganese intoxication. RYTARY is not for use in patients using nonselective monoamine oxidase inhibitors (MAO) inhibitors.

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"The FDA approval of RYTARY (pronounced rye-TAR-ee) is an important new development for the treatment of Parkinson's disease and provides an extended-release carbidopa-levodopa product that treats Parkinson's disease," said Fred Wilkinson , president and CEO, Impax Laboratories. "RYTARY is designed to address one of the most significant unmet needs for patients living with Parkinson's disease, which is to reduce the amount of time during the day when their symptoms are not adequately controlled."

"There are approximately one million Americans living with this chronic disease and we are pleased to offer this new therapy as a treatment option for those patients," added Wilkinson. "Today's approval of RYTARY is also a significant milestone for Impax because it is our first branded drug internally developed and approved for commercialization."

RYTARY contains immediate release and extended-release beads, with a specific amount of carbidopa and levodopa in a 1:4 ratio, and provides both initial and extended levodopa plasma concentrations after a single dose. RYTARY may be swallowed whole or, for patients who have trouble swallowing, the capsule may be opened and the beads sprinkled on applesauce and consumed immediately.

Impax expects the four strengths of RYTARY, 23.75mg/95mg, 36.25mg/145mg, 48.75mg/195mg, and 61.25mg/245mg (carbidopa/levodopa) to be available for commercial distribution in February 2015.

The RYTARY clinical program studied patients with early (levodopa-naive) to advanced Parkinson's disease in the U.S. and in Europe. In APEX-PD (Study 1), a trial that enrolled and randomized 381 levodopa-naive patients, the study met its primary efficacy endpoint of mean change from baseline in the sum of Unified Parkinson's Disease Rating Scale (UPDRS) Part II (activities of daily living) score and UPDRS Part III (motor skills) score for RYTARY versus placebo at Week 30 (or early termination).

In ADVANCE-PD (Study 2), a trial of 393 randomized patients with advanced Parkinson's disease having "off" time, the results showed treatment with RYTARY reduced the percentage of "off" time (36.9% to 23.8%) from baseline versus immediate-release carbidopa-levodopa (36.0% to 29.8%) during waking hours to end of study. RYTARY also increased "on" time without troublesome dyskinesia during waking hours versus baseline to end of study by 1.8 hours. Less "off" time was primary related to more "on" time without troublesome dyskinesia.

The most common adverse reactions with RYTARY in the APEX-PD trial (in at least 5% of patients and

more frequently than in placebo) were nausea, dizziness, headache, insomnia, abnormal dreams, dry mouth, dyskinesia, anxiety, constipation, vomiting, and orthostatic hypotension. The most common adverse reactions with RYTARY in the ADVANCE-PD trial (in at least 5% of patients and more frequently than an oral immediate-release carbidopa-levodopa) were nausea and headache.

**About Parkinson's disease**
Parkinson's disease is a chronic neurodegenerative movement disorder affecting approximately one million people in the U.S., with 50,000-60,000 new cases diagnosed each year in the U.S. alone. There is currently no known cure for Parkinson's.

**About RYTARY**

**IMPORTANT SAFETY INFORMATION**

- RYTARY is **contraindicated** in patients who are currently taking or have recently (within 2 weeks) taken a **nonselective monoamine oxidase (MAO) inhibitor** (e.g., phenelzine and tranylcypromine). Hypertension can occur if these drugs are used concurrently.
- Patients treated with levodopa (a component of RYTARY) have reported **falling asleep while engaged in activities of daily living**, including the operation of motor vehicles, which sometimes resulted in accidents. Although many of these patients reported somnolence while on levodopa, some perceived that they had no warning signs (sleep attack), such as excessive drowsiness, and believed that they were alert immediately prior to the event. Some of these events have been reported more than 1 year after initiation of treatment. Before initiating treatment with RYTARY, advise patients of the potential to develop drowsiness and specifically ask about factors that may increase the risk for **somnolence** with RYTARY such as concomitant sedating medications or the presence of a sleep disorder. Prescribers should consider discontinuing RYTARY in patients who report significant daytime sleepiness or episodes of falling asleep during activities that require active participation (e.g., conversations, eating, etc.). If a decision is made to continue RYTARY, patients should be advised not to drive and to avoid other potentially dangerous activities that might result in harm if the patients become somnolent.
- A symptom complex that resembles neuroleptic malignant syndrome (characterized by elevated temperature, muscular rigidity, altered consciousness, and autonomic instability), with no other obvious etiology, has been reported in association with rapid dose reduction, withdrawal of, or changes in dopaminergic therapy. Avoid sudden discontinuation or rapid dose reduction in patients taking RYTARY. If the decision is made to discontinue RYTARY, the dose should be tapered to reduce the risk of **hyperpyrexia and confusion**.
- **Cardiovascular ischemic events** have occurred in patients taking RYTARY. In patients with a history of myocardial infarction who have residual atrial, nodal, or ventricular arrhythmias, cardiac function should be monitored in an intensive cardiac care facility during the period of initial dosage adjustment.
- There is an increased risk for **hallucinations and psychosis** in patients taking RYTARY. Hallucinations present shortly after the initiation of therapy and may be responsive to dose reduction in levodopa. Hallucinations may be accompanied by confusion and sleep disorder (insomnia) and excessive dreaming. Abnormal thinking and behavior may present with one or more symptoms, including paranoid ideation, delusions, hallucinations, confusion, psychotic-like behavior, disorientation, aggressive behavior, agitation, and delirium.
  Because of the risk of exacerbating psychosis, patients with a major psychotic disorder should not be treated with RYTARY. In addition, medications that antagonize the effects of dopamine used to treat psychosis may exacerbate the symptoms of Parkinson's disease and may decrease the effectiveness of RYTARY.
- Case reports suggest that patients can experience **intense urges** to gamble, increased sexual urges,

intense urges to spend money, binge eating, and/or other intense urges, and the inability to control these urges while taking one or more of the medications, including RYTARY, that increase central dopaminergic tone and that are generally used for the treatment of Parkinson's disease. In some cases, although not all, these urges were reported to have stopped when the dose was reduced or the medication was discontinued. Because patients may not recognize these behaviors as abnormal, it is important for prescribers to specifically ask patients or their caregivers about the development of new or increased gambling urges, sexual urges, uncontrolled spending, or other urges while being treated with RYTARY. Consider a dose reduction or stopping the medication if a patient develops such urges while taking RYTARY.

- RYTARY can cause **dyskinesias** that may require a dosage reduction of RYTARY or other medications used for the treatment of Parkinson's disease.
- Treatment with RYTARY may increase the possibility of upper gastrointestinal hemorrhage in patients with a history of **peptic ulcer** and may cause increased intraocular pressure in patients with **glaucoma**.
- RYTARY should be used during **pregnancy** only if the potential benefit justifies the potential risk to the fetus. Caution should be exercised when RYTARY is administered to a **nursing** woman.

**Overdosage**

- The acute symptoms of levodopa/dopa decarboxylase inhibitor overdosage can be expected to arise from dopaminergic overstimulation (cardiovascular and CNS disturbances).

**Drug Interactions:**

- Monitor patients taking **selective MAO-B inhibitors** and carbidopa-levodopa. The combination may be associated with orthostatic hypotension. RYTARY should be co-administered cautiously with: **dopamine D2 antagonists** (**metoclopramide**), **isoniazid**, and **iron salts**.
- **RYTARY should not be chewed, divided, or crushed.**

**About Impax Pharmaceuticals**
Impax Pharmaceuticals is the branded products division of Impax Laboratories, Inc. Impax Pharmaceuticals is focused on targeting significant unmet needs, with a primary focus on developing treatments for neurological disorders. For more information, please visit its web site at www.impaxpharma.com.

**About Impax Laboratories, Inc.**
Impax Laboratories, Inc. (Impax) is a technology based specialty pharmaceutical company applying its formulation expertise and drug delivery technology to the development of controlled-release and specialty generics in addition to the development of central nervous system disorder branded products. Impax markets its generic products through its Global Pharmaceuticals division and markets its branded through the Impax Pharmaceuticals division. Additionally, where strategically appropriate, Impax develops marketing partnerships to fully leverage its technology platform and pursues partnership opportunities that offer alternative dosage form technologies, such as injectables, nasal sprays, inhalers, patches, creams, and ointments. For more information, please visit the Company's web site at: www.impaxlabs.com.

***"Safe Harbor" statement under the Private Securities Litigation Reform Act of 1995:***
To the extent any statements made in this news release contain information that is not historical; these statements are forward-looking in nature and express the beliefs and expectations of management. Such statements are based on current expectations and involve a number of known and unknown risks and uncertainties that could cause the Company's future results, performance, or achievements to differ significantly from the results, performance, or achievements expressed or implied by such forward-looking statements. Such risks and uncertainties include, but are not limited to: fluctuations in revenues and

operating income; the Company's ability to promptly correct the issues raised in the warning letter and Form 483 observations received from the FDA; the Company's ability to successfully develop and commercialize pharmaceutical products in a timely manner; reductions or loss of business with any significant customer; the impact of consolidation of the Company's customer base; the impact of competition; the substantial portion of our total revenues derived from sales of a limited number of products; the Company's ability to sustain profitability and positive cash flows; any delays or unanticipated expenses in connection with the operation of the Company's manufacturing facilities; the effect of foreign economic, political, legal, and other risks on the Company's operations abroad; the uncertainty of patent litigation and other legal proceedings; the increased government scrutiny on the Company's agreements with brand pharmaceutical companies; product development risks and the difficulty of predicting FDA filings and approvals; consumer acceptance and demand for new pharmaceutical products; the impact of market perceptions of the Company and the safety and quality of the Company's products; the Company's determinations to discontinue the manufacture and distribution of certain products; the Company's ability to achieve returns on its investments in research and development activities; the Company's inexperience in conducting clinical trials and submitting new drug applications; the Company's ability to successfully conduct clinical trials; the Company's reliance on third parties to conduct clinical trials and testing; the Company's lack of a license partner for commercialization of IPX066 outside of the United States; impact of illegal distribution and sale by third parties of counterfeits or stolen products; the availability of raw materials and impact of interruptions in the Company's supply chain; the Company's policies regarding returns, allowances and chargebacks; the use of controlled substances in the Company's products; the effect of current economic conditions on our industry, business, results of operations and financial condition; disruptions or failures in the Company's information technology systems and network infrastructure; the Company's reliance on alliance and collaboration agreements; the Company's reliance on licenses to proprietary technologies; the Company's dependence on certain employees; the Company's ability to comply with legal and regulatory requirements governing the healthcare industry; the regulatory environment; the Company's ability to protect its intellectual property; exposure to product liability claims; risks relating to goodwill and intangibles; changes in tax regulations; the Company's ability to manage growth, including through potential acquisitions; the Company's ability to meet expectations regarding the timing and completion of the proposed transaction with Tower Holdings Inc. and Lineage Therapeutics Inc., the Company's ability to consummate such proposed transaction; the conditions to the completion of such proposed transaction (including the receipt of the regulatory approvals required for the transaction not being obtained on the terms expected or on the anticipated schedule), the integration of the acquired business by the Company being more difficult, time-consuming or costly than expected, operating costs, customer loss and business disruption (including, without limitation, difficulties in maintaining relationships with employees, customers, clients or suppliers) being greater than expected following the proposed transaction, the retention of certain key employees of the acquired business being difficult, the Company's and the acquired business's expected or targeted future financial and operating performance and results, the combined company's capacity to bring new products to market, and the possibility that the Company may be unable to achieve expected synergies and operating efficiencies in connection with the proposed transaction within the expected time-frames or at all and to successfully integrate the acquired business, the restrictions imposed by the Company's credit facility; uncertainties involved in the preparation of the Company's financial statements; the Company's ability to maintain an effective system of internal control over financial reporting; the effect of terrorist attacks on the Company's business; the location of the Company's manufacturing and research and development facilities near earthquake fault lines; expansion of social media platforms and other risks described in the Company's periodic reports filed with the Securities and Exchange Commission. Forward-looking statements speak only as to the date on which they are made, and the Company undertakes no obligation to update publicly or revise any forward-looking statement, regardless of whether new information becomes available, future developments occur or otherwise.

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