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Newly published Phase III data show Novartis drug Sandostatin[®] LAR Depot reduced risk of disease progression by 66% in advanced NET patients

- *Study published in Journal of Clinical Oncology demonstrate antitumor benefit of Sandostatin LAR in advanced midgut neuroendocrine tumor (NET) patients*
- *Data show Sandostatin LAR more than doubled time without tumor progression for median of 14 months versus six months with placebo*
- *National Comprehensive Cancer Network (NCCN) treatment guidelines for advanced NET patients updated based on these data*

East Hanover, N.J., October 1, 2009 — Data published in the *Journal of Clinical Oncology* show that patients with advanced neuroendocrine tumors (NET) of the midgut who were treated with Sandostatin[®] LAR Depot (octreotide acetate for injectable suspension) experienced a 66% reduction in risk of disease progression versus placebo¹. Sandostatin LAR is indicated to treat the diarrhea and flushing episodes associated with advanced carcinoid tumors².

These data are from the Phase IIIb study PROMID. In the study, patients receiving octreotide LAR more than doubled time without tumor progression for a median of 14 months compared with a median of six months for those who received placebo¹.

Neuroendocrine tumors are the second most common gastrointestinal malignancy after colon cancer³. These tumors originate from cells that have roles both in the endocrine and nervous systems, and they can be either functioning or non-functioning⁴. Functioning NET causes the symptoms of carcinoid syndrome, including flushing, diarrhea and wheezing. The majority of NET are non-functioning, which means they do not cause symptoms of carcinoid syndrome³. Once a NET has spread from its point of origin to other parts of the body a patient has few treatment options⁵.

"PROMID is a placebo-controlled, randomized trial that showed octreotide LAR can control tumor growth in all patients with NET of the midgut whether or not they experience symptoms," said PROMID lead investigator Professor Rudolf Arnold, Philipps-University, Marburg, Germany. "These are promising data for patients with NET who face limited treatment options."

The PROMID study showed antitumor benefit in patients with functioning and non-functioning tumors resulting from treatment with octreotide LAR. In an analysis of patients with non-functioning tumors, time to tumor progression for patients receiving octreotide LAR was 28.8 months versus 5.9 months for those on placebo (hazard ratio=0.25 [95% confidence interval 0.10-0.59]). For patients with functioning tumors, time to tumor

progression for patients receiving octreotide LAR was 14.3 months and 5.5 months for those on placebo (hazard ratio=0.23 [95% confidence interval 0.09 to 0.57])¹.

Earlier this year, the NCCN updated its clinical practice guidelines based on the results of PROMID. The NCCN guidelines now recommend the use of octreotide LAR as a treatment option for all metastatic, unresectable midgut NET patients, regardless of symptoms⁶.

"For more than a decade, octreotide LAR has been a cornerstone of NET treatment for the symptoms of flushing and diarrhea associated with carcinoid syndrome," said David Epstein, President and CEO, Novartis Oncology, Novartis Molecular Diagnostics. "The findings of the PROMID trial are critical because they show octreotide LAR also has the potential to control tumor growth and provide the benefit of treatment to even more patients with an unmet medical need."

About PROMID

PROMID (Placebo-controlled, double-blind, prospective Randomized study on the effect of Octreotide LAR in the control of tumor growth in patients with metastatic neuroendocrine MIDgut tumors) is a Phase IIIb study conducted at 18 sites in Germany to evaluate the antitumor effect of octreotide LAR in patients regardless of symptoms. The study included 85 patients who were treated with either octreotide LAR or placebo until tumor progression. All participants were treatment-naïve, had locally inoperable or metastatic NET with the primary tumor in the midgut and were without curative therapeutic options. The study was sponsored by Novartis¹.

The results of the pre-planned interim analysis now published in the *Journal of Clinical Oncology* were first presented at the Gastrointestinal Cancer Symposium of the American Society of Clinical Oncology (ASCO GI) in January. An updated analysis with longer patient follow-up was presented earlier this year at the annual meeting of the American Society of Clinical Oncology (ASCO) in Orlando, Florida. The updated results confirm that octreotide LAR, when compared to placebo, more than doubled time without tumor growth (15.6 months vs. 5.9 months) and reduced the risk of disease progression by 67% (hazard ratio=0.33 with 95% confidence interval 0.19 to 0.55; P=0.00017)⁷.

The safety profile observed in the PROMID study was consistent with that seen in previous studies of octreotide LAR. The most frequently observed serious adverse events affected the gastrointestinal tract (octreotide LAR arm: n=6, placebo arm n=8), the hematopoietic system (octreotide LAR arm: n=5, placebo arm n=1) and the general health status (fatigue, fever; octreotide LAR arm: n=8, placebo arm n=2). Serious adverse events occurred in 11 octreotide LAR-treated patients and 10 placebo recipients. Discontinuation of treatment due to adverse effects occurred in five of 42 patients in the octreotide LAR and none of the 43 patients in the placebo arm.

About neuroendocrine tumors

There are many different types of NET, which can occur throughout the body⁸. However, most are found in the digestive system and are collectively called gastroenteropancreatic neuroendocrine tumors (GEP-NET)^{4,9}. Carcinoid tumors and pancreatic NET are types of GEP-NET³. Although it is considered a rare cancer, the incidence of NET is on the rise and more prevalent than originally reported⁸.

About Sandostatin LAR Depot

Sandostatin LAR Depot is a long-acting, injectable depot formulation of octreotide acetate that is approved for the treatment of diarrhea/flushing episodes associated with advanced carcinoid tumors and profuse watery diarrhea associated with VIP-secreting tumors.

Sandostatin LAR is a somatostatin analogue which exerts similar pharmacologic effects on the human body as the natural hormone somatostatin. However, octreotide is even more potent than somatostatin at inhibiting growth hormone, glucagon and insulin. Like somatostatin, it also suppresses LH response to GnRH, decreases splanchnic blood flow and inhibits the release of serotonin, gastrin, vasoactive intestinal peptide, secretin, motilin and pancreatic polypeptide. Based on these attributes, octreotide has been used to treat symptoms associated with metastatic carcinoid tumors (flushing and diarrhea) and vasoactive intestinal peptide (VIP) secreting adenomas (watery diarrhea)¹.

Sandostatin LAR is not indicated as a treatment for tumor control. The clinical trials that supported approval of Sandostatin LAR did not study effect on tumor size or rate of growth¹.

The active ingredient in Sandostatin LAR, octreotide acetate, was approved in the United States in October of 1988. In November of 1998, the FDA approved the long-acting formulation of octreotide acetate which Novartis markets as Sandostatin LAR. For more than a decade, Sandostatin LAR has achieved a long-standing track record of sustained efficacy with a well-established safety profile¹.

Sandostatin LAR Depot important safety information

The most frequently reported drug-related adverse events were biliary disorders (62%), gastrointestinal disorders (14% to 38%), and injection-site pain (20% to 50%). Hypoglycemia (4%), hyperglycemia (27%), sinus bradycardia (19%), conduction abnormalities (9%), and arrhythmias (3%) have been reported. Additional adverse reactions identified in clinical studies include nausea, abdominal pain, gas, constipation, vomiting, pain on injection, high or low blood sugar levels and slow or irregular heart rate. Many patients developed gallstones, although few patients required treatment¹.

For full prescribing information, please visit www.us.sandostatin.com.

Disclaimer

The foregoing release contains forward-looking statements that can be identified by terminology such as “risk,” “promising,” “potential,” or similar expressions, or by express or implied discussions regarding potential new indications or labeling for Sandostatin LAR, or regarding potential future revenues from Sandostatin LAR. You should not place undue reliance on these statements. Such forward-looking statements reflect the current views of management regarding future events, and involve known and unknown risks, uncertainties and other factors that may cause actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. There can be no guarantee that Sandostatin LAR will be submitted or approved for any additional indications or labeling in any market. Nor can there be any guarantee that Sandostatin LAR will achieve any particular levels of revenue in the future. In particular, management’s expectations regarding Sandostatin LAR could be affected by, among other things, unexpected clinical trial results, including unexpected regulatory actions or delays or government regulation generally; unexpected new clinical data and unexpected additional analysis of existing clinical data; the company’s ability to obtain or maintain patent or other proprietary intellectual property protection; competition in general; government, industry and general public pricing pressures; the impact that the foregoing factors could have on the values attributed to the Novartis Group’s assets and liabilities as recorded in the Group’s consolidated balance sheet, and other risks and factors referred to in Novartis AG’s current Form 20-F on file with the US Securities and Exchange Commission. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those anticipated, believed, estimated or expected. Novartis is providing the information in this

press release as of this date and does not undertake any obligation to update any forward-looking statements contained in this press release as a result of new information, future events or otherwise.

About Novartis

Located in East Hanover, New Jersey, Novartis Pharmaceuticals Corporation is an affiliate of Novartis AG which provides healthcare solutions that address the evolving needs of patients and societies. Focused solely on healthcare, the Novartis Group offers a diversified portfolio to best meet these needs: innovative medicines, preventive vaccines, diagnostic tools, cost-saving generic pharmaceuticals and consumer health products. The Novartis Group is the only company with leading positions in each of these areas. In 2008, the Group's continuing operations achieved net sales of USD 41.5 billion and net income of USD 8.2 billion. Approximately USD 7.2 billion was invested in R&D activities throughout the Group. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 99,000 full-time-equivalent associates and operate in more than 140 countries around the world. For more information, please visit <http://www.us.novartis.com>.

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