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New Zelnorm® data demonstrate relief of multiple symptoms of dysmotility-type dyspepsia

- *Dysmotility-type dyspepsia causes gastrointestinal discomfort that can be chronic and disruptive for patients*
- *Clinical data show potential benefit of Zelnorm for women with this common digestive disorder¹*
- *No currently approved products available to treat this widespread condition*

Basel, October 23, 2006 – The gastrointestinal medicine Zelnorm® (tegaserod maleate) has demonstrated potential benefits in helping patients with the multiple symptoms of a common digestive disorder called dysmotility-type dyspepsia¹, according to new Phase III data presented at the American College of Gastroenterology (ACG) Annual Scientific Meeting.

Dysmotility refers to abnormal movement of food through the stomach, with dysmotility-type dyspepsia a common digestive condition characterized by multiple symptoms that include bloating, an excessive and uncomfortable feeling of fullness after eating, and extreme fullness soon after the start of a meal.

The condition is a form of functional dyspepsia, which is estimated to affect about 25% of the adult population in the United States^{2,3}. No currently approved medications are available to treat dysmotility-type dyspepsia or its associated symptoms, which can be chronic and disruptive.

"These multiple symptoms have a very significant impact on patients' lives," said Loren Laine, MD Professor of Medicine, University of Southern California School of Medicine. "For patients with moderate to severe symptoms the results of these studies are promising and suggest a benefit for tegaserod."

Zelnorm is already approved in 55 countries for treatment of irritable bowel syndrome with constipation (IBS-C) and in 20 countries for chronic idiopathic constipation.

Pooled data from the two pivotal studies (n=2,667) show a positive benefit with Zelnorm treatment versus placebo. Benefits were seen in the dysmotility-type dyspepsia symptoms including early satiety (extreme sensation of fullness after a small amount of food), post-prandial fullness (uncomfortable feeling of fullness after a meal) and bloating.

The data showed a statistically significant treatment benefit with Zelnorm (p<0.05) for the primary endpoints¹. In patients with more severe baseline dysmotility symptoms, Zelnorm showed an enhanced treatment effect versus placebo. Further research is needed to understand the mechanism of action of Zelnorm in patients with dysmotility-type dyspepsia.

“We know that Zelnorm uniquely treats the major underlying cause of dysmotility in the gastrointestinal tract. For the first time, these new data suggest Zelnorm has the potential to treat dysmotility-type dyspepsia,” commented James Shannon, MD, Global Head of Development at Novartis Pharma AG. “Millions of patients currently rely on Zelnorm to relieve irritable bowel syndrome with constipation and chronic constipation, and these new study results may offer hope of relief for those living with symptoms of dysmotility-type dyspepsia.”

About the dyspepsia trials

A total of 2,667 women age 18 or older were randomized in the two studies. The co-primary endpoints for each study were the percentage of days with satisfactory relief of dyspepsia symptoms and the composite average daily symptom score. The symptom score endpoints were measured using a 7-point Likert scale (from 1 = no discomfort at all to 7 = very severe discomfort). Patients were excluded from these studies if they had concomitant heartburn, irritable bowel syndrome or gastroesophageal reflux disease. All patients included had to have at least mild dyspepsia¹.

Study 1 showed a statistically significant improvement with Zelnorm treatment compared to placebo for the endpoints of the mean percentage of days with satisfactory relief (Zelnorm 32.24% vs. placebo 26.63%, $p=0.0002$) and the composite average daily symptom score (Zelnorm 3.14 vs. placebo 3.35, $p<0.0001$).

Study 2 showed a trend in favor of Zelnorm compared to placebo for both endpoints – percentage of days with satisfactory relief (Zelnorm 31.87% vs. placebo 29.36%, $p=0.0662$) and composite average daily symptom score (Zelnorm 3.15 vs. placebo 3.23, $p=0.0936$), although statistical significance was not achieved¹.

The adverse event profiles in both studies were consistent with the established safety and tolerability profile. The most common adverse event was diarrhea, which occurred in about 19% of Zelnorm-treated patients compared to 4-5% of placebo patients. These events tended to occur in the first week of therapy, were transient, self-limiting and did not require discontinuation. Study discontinuations due to diarrhea were low, ranging from 3-5%. There were no serious consequences of diarrhea reported in the pivotal studies¹.

About Zelnorm

Zelnorm, a promotility agent, is the first in a class of medications known as serotonin-4 receptor agonists (5HT₄ agonists), specifically developed to treat the multiple symptoms associated with dysmotility disorders like irritable bowel syndrome with constipation. By activating 5HT₄ receptors in the gastrointestinal tract, Zelnorm normalizes delayed motility and reduces sensitivity of the intestinal tract^{4,5,6,7}.

In clinical studies, significantly more patients experienced a general relief of symptoms when treated with Zelnorm, such as a decrease in abdominal pain, bloating and constipation. In most patients, the onset of relief occurred within just one week^{8,9,10,11,12}. The medication has been shown to be well tolerated and shows a side effect profile similar to that of placebo, with the exception of diarrhea^{6,8,9,10}. The majority of patients reporting diarrhea had a single episode, typically occurring in the first week of treatment and resolving with continued therapy.

Zelnorm, discovered and developed by Novartis, is approved for the treatment of irritable bowel syndrome with constipation in more than 55 countries including Australia, Switzerland, Canada, the US, Mexico, China and Brazil. Zelnorm is also approved for the treatment of chronic constipation in more than 20 countries including the US, Canada and Mexico. Novartis markets the product under the trade name Zelnorm (tegaserod maleate) in the US, Canada, Philippines and South Africa; and as Zelmac (tegaserod) in Switzerland, Latin America and the Asia-Pacific region.

Disclaimer

The foregoing press release contains forward-looking statements that can be identified by the use of forward-looking terminology such as “can be”, “potential”, “may,” or similar expressions, or by express or implied discussions regarding potential future regulatory filings, approvals or future sales of Zelnorm. Such forward-looking statements 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 Zelnorm will be approved for any additional indications, that Zelnorm will be brought to market in any additional countries, or will reach any particular level of sales. In particular, management’s expectations regarding Zelnorm could be affected by, among other things, unexpected clinical trial results, including new clinical data and additional analysis of existing clinical data; unexpected regulatory actions or delays or government regulation generally; competition in general; government, industry, and general public pricing pressures; the company’s ability to obtain or maintain patent or other proprietary intellectual property protection; as well as the additional factors discussed in Novartis AG’s Form 20-F filed 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 described herein as anticipated, believed, estimated or expected. Novartis is providing this information as of this date and does not undertake any obligation to update any forward-looking statements contained in this document as a result of new information, future events or otherwise.

About Novartis

Novartis AG (NYSE: NVS) is a world leader in offering medicines to protect health, treat disease and improve well-being. Our goal is to discover, develop and successfully market innovative products to treat patients, ease suffering and enhance the quality of life. Novartis is the only company with leadership positions in both patented and generic pharmaceuticals. We are strengthening our medicine-based portfolio, which is focused on strategic growth platforms in innovation-driven pharmaceuticals, high-quality and low-cost generics, human vaccines and leading self-medication OTC brands. In 2005, the Group’s businesses achieved net sales of USD 32.2 billion and net income of USD 6.1 billion. Approximately USD 4.8 billion was invested in R&D. Headquartered in Basel, Switzerland, Novartis Group companies employ approximately 99,000 people and operate in over 140 countries around the world. For more information, please visit <http://www.novartis.com>.

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