Boston Scientific Completes Enrollment of Europe Placebo-Controlled Study of Enteryx™ Technology for Treatment of GERD Symptoms

Boston Scientific Corporation announced that it has completed enrollment in a European multi-center placebo-controlled randomized trial to confirm the safety and effectiveness of the Enteryx Technology in improving symptoms commonly associated with gastroesophageal reflux disease (GERD). The multi-center study enrolled 60 patients at four centers in Belgium, Italy and Germany. As part of the study protocol, patients will receive follow-up assessments at three, six and 12 months post-procedure.

Enteryx is an endoscopic, injectable copolymer that offers an alternative for the treatment of gastroesophageal reflux disease (GERD) symptoms in patients responding to and requiring daily pharmacological therapy with proton pump inhibitors (PPIs). The Enteryx solution is designed to help improve the mechanical function of the Lower Esophageal Sphincter (LES) and has been rigorously tested to show safety and effectiveness.

"At one year Enteryx was shown to reduce significantly or eliminate PPI use in about three out of four patients enrolled in U.S. and European multi-center trials," said Jacques Deviere, M.D., Chairman of the Department of Gastroenterology at Erasme Hospital in Brussels, Belgium. "Preliminary results at two years indicate good durability of effectiveness."

Boston Scientific is also currently enrolling patients in a similar, U.S.-based multi-center, randomized, controlled study.

Given Imaging Announces Expanded Coverage Policy from Aetna

Policy Also Provides Reimbursement of Capsule Endoscopy For Suspected Crohn's Disease

Given Imaging announced that Aetna has updated its reimbursement policy for Capsule Endoscopy to include also the initial diagnosis of suspected Crohn's disease following inconclusive conventional tests such as small-bowel follow-through and upper and lower endoscopy. This decision expands Aetna's original policy of April 2003 which covered Capsule Endoscopy only in patients with suspected bleeding

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following inconclusive upper and lower gastrointestinal endoscopies. The updated policy is already in effect.

An Increasing Incidence of HIV/HBV Co-infection Provides Pharma Companies with the Opportunity to Fill the Gap in HIV Market

A new report from independent market analyst, Datamonitor's (DTM.L), reveals that the rate of Hepatitis B (HBV) co-infection in HIV infected individuals is increasing among the seven major markets (Japan, US, France, Italy, UK, Germany, Spain), with an average incidence of 7%. The advent of Highly Active Antiretroviral Therapy (HAART) has led to increased longevity in those infected with HIV and shared epidemiological risk increases the likelihood of these individuals contracting HBV. Although HBV has little impact on HIV disease progression, HIV renders HBV more aggressive and frequent, with co-infected individuals eight times more likely to die of liver damage-related mortality. Datamonitor reveals that inadequate diagnosis of concurrent disease states, lack of effective HBV treatment and HAART hepatoxicity all have a great impact on the effective management of this niche population. Datamonitor recommends that development of HBV antivirals, preferably with dual HIV and HBV efficacy, would address the obvious gap in treating this co-morbid population, providing an additional opportunity for companies to capitalize on the HIV mono-infected market.

One of Datamonitor's key findings was the lack of awareness and recognition of this co-infected state by both physicians and patients. Early diagnosis of the co-morbid population is affected by physicians' ignorance mainly due to the scarcity of comprehensive treatment guidelines. Datamonitor also found that, within different markets, co-morbid patients were presenting and receiving treatment through a variety of routes within their respective healthcare systems; an additional issue with negative implications for patients' effective management. The report warns that concurrent early diagnosis of both HIV and HBV disease states is essential to increasing the life span of this co-morbid population. Confirming the presence of both viruses ensures optimum treatment from the onset, thus improving patient prognosis at later stages.

HBV co-infection acts as an additional economic burden to an already expensive HIV HAART regimen (approximately $10,000 per patient in the US). It is therefore more cost-effective to vaccinate the HIV/HBV co-infected population, rather than manage HBV infection with expensive antiviral and immunomodulator therapies. Although HBV vaccines have reduced efficacy in HIV-infected patients, they could still diminish co-infection prevalence.

Based on key opinion leader findings, Datamonitor suggests several actionable points, the first being that the majority of those co-infected with HIV/HBV, i.e. HIV-infected high-risk groups such as intravenous drug users (IVDUs)), be further targeted for diagnosis, vaccination and treatment to minimize infection. This could also be extended to new immigrants in Western regions. Although immigration of HBV infected individuals from endemic countries was thought to have little impact on the general population, it is likely to affect those same high-risk groups. Western markets, such as the UK, with a high degree of immigration from sub-Saharan Africa should therefore reconsider their HBV vaccination guidelines. They should also be aware of the "relapse" in the male homosexual population with regard to the transmission of parenteral viruses, although this is thought to be relatively rare for HBV.

The main aim of HBV mono and co-infection treatment is the suppression of viral replication, improving liver histology, and the prevention of hepatocellular carcinoma. Ultimately the goal is to achieve complete clearance or eradication of the HBV virus and induce an antibody specific immune response. Datamonitor revealed that currently marketed HBV antivirals only achieve seroconversion in approximately 10% of the HBV mono-infected population and this figure will be significantly lower for the co-morbid populace. In response to this need, a number of companies including Gilead and Idenix/Novartis have recognized an emerging market for increased HBV potency but more importantly, agents capable of seamless integration with HAART regimes. This dynamic is driven further by the current unsuitability of immunomodulators and the increased product saturation of the HIV mono-infected market.

The dual targeting ability of many existing HIV therapeutics such as Gilead's Viread and Emtriva provide

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opportunities for product lifecycle management with potential tailoring for the treatment of both HBV mono and co-infection. This strategy has been employed successfully for GSK's Epivir and may be extended to MIV-310, a dual-spectrum antiviral announced as part of a recent agreement with Medivir and Boehringer Ingleheim. Idenix/Novartis are taking a different approach, focusing on the mass-HBV mono-infected population with potent developmental agents such as Telbuvidine. Aside from mono-infection, manufacturers should be increasingly aware of the co-morbid population's specific needs and that well-defined clinical studies on these groups could provide them with a competitive advantage outside mono-infected populations.

In conjunction with potential commercial support and advocacy of HBV vaccination, Datamonitor believes that with the advent of newer more potent HBV therapeutic agents, targeting countries where HBV is endemic could be profitable with the preparation of a vaccine-like high volume/low cost model. A large-scale production of an efficacious antiviral with eradication rates of 25%–50% provided at low cost via collaborations with organizations such as the World Health Organization (WHO) could achieve this goal.

Wyeth Receives FDA Approval of New Formulation for Protonix® I.V.

New Formulation Provides Filterless Administration

Wyeth Pharmaceuticals, announced that the U.S. Food and Drug Administration (FDA) approved the reformulation of the stomach acid suppressant, Protonix® I.V. (pantoprazole sodium) for Injection. The reformulation eliminates the need for an in-line filter, a previously required extra step in an already time-sensitive procedure to administer the medication to patients requiring immediate acid suppression.

Protonix is the first and only proton pump inhibitor (PPI) in the United States to be offered in both oral and intravenous (I.V.) formulations.

The new formulation will replace the existing PROTONIX I.V. formulation, which has been used clinically for seven years in more than five million patients worldwide.

The new formulation has been approved for administration either as a 2-minute or 15-minute infusion. Protonix I.V. received FDA approval in December 2003 for administration as a 2-minute infusion. This alternative infusion approach may reduce drug preparation time and administration costs in hospitals, since the intravenous admixture bag can be replaced with a less expensive syringe for administration.

Power Medical Interventions™ Introduces Improved Endosurgical Stapler

New CS29 Enhances SurgASSIST Platform

Power Medical Interventions™, designer and manufacturer of computer-mediated surgical stapling products, has introduced the new and improved CS29 circular stapler/cutter digital loading unit® (DLU). The CS29 is one of many DLU®s that provide the surgical action for the company's revolutionary SurgASSIST™ system. SurgASSIST™ is an integrated, computer-mediated surgical platform used in a broad range of open and endosurgical procedures.

"In November, we voluntarily recalled the CS29 due to reports of inconsistent performance in thick tissue applications," said Mike Whitman, president and CEO of PMI. "Thick tissue always presents a challenge to endosurgical staplers. We analyzed each part under every conceivable firing condition and found that heavy firing loads caused occasional anvil slippage and staple misalignment."

"Once the problem was identified, our team of engineers redesigned and repeatedly tested the product in multiple applications to ensure that the new and improved CS29 circular stapler will deliver superior performance and reliability under the most demanding and high-stress conditions. The net result of our efforts is that the average latch retention strength is now 830 lbs, up from 480 lbs. with the earlier version." Colorectal surgeons around the world confirmed the improved reliability of the CS29 through dozens of procedures performed in pre-clinical trials and more than 100 clinical firings since the re-launch.

The modified CS29 DLU® began shipping on March 6, with the first deliveries made to Columbia Presbyterian, Sloan-Kettering, and the Hospital of the University of Pennsylvania (HUP). The enhanced CS29 has now been used in hundreds of procedures, and every firing to date has been flawless. PMI will continue to

closely monitor the CS29's performance, and expects outstanding reliability and effectiveness from the unit.

Fired remotely by the surgeon, the CS29 DLU® enables the SurgASSIST™ computer-mediated surgical platform to create end-to-end anastomoses more quickly, and with more precise staple formation than manually-fired devices. In addition, remote controlled, computer-mediated firing decreases movement at the surgical site, producing more consistent results than traditional stapling and cutting devices. To accommodate a vast array of applications, the CS29 is one of several DLU®s from PMI that includes straight linear stapler/cutters, right angle linear stapler/cutters and circular stapler/cutters.

For more information on PMI and its selection of computer-mediated surgical stapling products please visit the company's Web site at www.pmi2.com.

NCCN Announces Release of Gastrointestinal Stromal Tumors (GIST) Task Force Report

The National Comprehensive Cancer Network has introduced The NCCN Gastrointestinal Stromal Tumors (GIST) Task Force Report. The report, an expansion on The NCCN Sarcoma Clinical Practice Guidelines in Oncology, outlines the current thinking about the optimal management of patients with GIST. Though an uncommon cancer, GIST is increasingly recognized after experts reported that imatinib (Gleevec®, Novartis Pharmaceuticals) an oral cancer therapy which targets a molecular switch important to the tumor cells, could induce dramatic remissions and prolong survival for patients with advanced GIST.

"The clinical care of patients with GIST has changed radically in the past few years thanks to the rapid evolution of research translating into new and effective therapeutic strategies," said George D. Demetri, MD, Chair, GIST Task Force and Director of the Center for Sarcoma and Bone Oncology at Harvard's Dana-Farber Cancer Institute. "The GIST Task Force Report represents the work of expert physicians from several disciplines, such as pathology, surgery, medical oncology, and radiology. Together, we have outlined the most effective approach for optimal management of GIST patients. Our aim is to increase awareness of the tremendous changes which have developed in such a short time in our approach to patients with GIST, and to identify opportunities for future research to improve outcomes further."

Preliminary recommendations of the GIST Task Force Report were presented at the NCCN ninth annual conference: Clinical Practice Guidelines and Outcomes Data in Oncology in Hollywood, Florida. The complete report will be published as a supplement to the May 2004 issue of the *Journal of the National Comprehensive Cancer Network (JNCCN)*.

GIST is the most common form of gastrointestinal (GI) sarcoma, a life-threatening cancer of the GI tract. Recent data suggest that there are as many as 4,500 to 6,000 new cases of GIST per year in the United States. The introduction of effective molecularly targeted therapy has dramatically improved the outcomes for patients diagnosed with GIST.

"The NCCN was pleased to be able to bring together experts from across the USA and Canada to analyze and discuss the evidence supporting the newest and best standards for management of this disease," said Joan S. McClure, MS, Vice President, Clinical Information and Publications for NCCN. "Advances in pathologic diagnosis, imaging technology, and treatment modalities have merged to significantly change the way clinicians of multiple specialties interact to care for patients with GIST as a coordinated team."

The task force report describes the cooperative multidisciplinary effort among medical oncology, surgery, pathology, and other specialties that is necessary to achieve the best possible results, which include reducing the incidence and risks of recurrent disease, optimizing disease control, improving quality of life by minimizing surgery that might impair function, and prolonging survival.

The National Comprehensive Cancer Network (NCCN), an alliance of 19 of the world's leading cancer centers, is an authoritative source of information to help patients and health professionals make informed decisions about cancer care. Through the collective expertise of its member institutions, the NCCN develops, updates, and disseminates a complete library of clinical practice guidelines. These guidelines are the standard for clinical policy in oncology.

For more information visit www.nccn.org.

Mayo Clinic Gastroenterology and Hepatology Board Review

Hauser SC, Pardi DS and Poterucha JJ, eds
CRC Press. 2003; ISBN: 0-8493-2054-2; $89.95

This book comprises eight sections organized by organ and is amply illustrated. There are about 20 questions at the end of each section. Each section comprises 4–6 chapters, each of which is a concise and practical review of a specific condition. Each section is authored by a clinician affiliated with the Mayo Clinic, several of whom have particular interests in the subspecialty areas, thus bringing a broad range of expertise to this undertaking.

The clinical focus of this book is readily apparent both in the organization of material and the use of clinical vignettes based questions at the end of each section. There is emphasis on clinical presentation, diagnosis, and management of commonly encountered conditions (both in the real world and on board questions). Questions are used to reinforce concepts reviewed in each section—occasionally this means a similar question is paraphrased differently later on in the section. The liberal use of tables and cartoons to illustrate steps in diagnosis and management are also helpful for reinforcement which is critical in a board review.

As in any book that deals with endoscopy, pictures are an important concern. The numerous pictures used to illustrate each chapter are good reminders of the classic endoscopic appearance of common and some less common gastrointestinal conditions. Particularly noteworthy are the chapters on Esophageal Motility which has a number of manometric recordings illustrating the classical esophageal dysmotility syndromes and the chapter on Endoscopic Ultrasound, also amply illustrated with representative pictures.

In comparison to other board review tools, such as the DDSEP, this book is smaller in size, more information dense, and much more clinically oriented. There is perhaps less emphasis on physiological mechanisms and dysfunction, which are reviewed in less detail. A minor drawback is the absence of a CD-ROM, which may dissuade people who desire a more interactive medium. As always, one can quibble about poorly written or ambiguous questions—though these are at a minimum in this book.

In summary, this is a compact, information dense book that delivers a good basic overview of the subject. The size, organization, and style of writing make it an easy read, and it thus makes the business of "getting ready for boards" much more manageable. However, it does not purport to be a replacement for encyclopedic textbooks or reference books or even a summary of the latest developments in the field. This is a book that is targeted to, and perhaps best meets the needs of, the fellow in training preparing for certification or a physician in practice who would like a "refresher course" in basic gastroenterology, hepatology, and nutrition.

Priya Balasubramanian (Sacramento, CA)

The Esophagus, 4th Ed

Castell DO and Richter JE, eds
Lippincott Williams and Wilkins; Philadelphia, 2004
ISBN: 0-7817-4199-8; $199.95

Castell and Richter have virtually rewritten a good portion of this book by getting new authors to review and rewrite more than half the chapters. In addition they have added several new chapters such as Endoscopic Treatment of GERD, H. pylori and GERD, GERD in Children, and Multichannel Intraluminal Impedance. The information provided is well balanced, being evenly distributed between physicians, surgeons, and physiologists.

The book is well illustrated with photographs, X-rays, and endoscopic photos. Most of the black and white photos have been well marked with arrows and other marking devices to clearly demonstrate the point being illustrated. There are two sets of color plates in the body of the book but color photographs are not added in the chapters. Some of the color prints are provided with arrows to highlight the key points. The chapters are well referenced often with references as late as 2002.

This book remains the bible for those with an interest in esophageal anatomy , physiology, and diseases and the treatment of those diseases. It is a superb undertaking and a tribute to the lifelong dedication of Castell and Richter to making the esophagus and its diseases understood by us all. The book is a must for anyone interested in the esophagus. It should be on the shelf of every fellowship program's library and in most hospital libraries.

George Meyer (Sacramento, CA)

George W. Meyer, M.D., Book Editor, is on the Editorial Board of *Practical Gastroenterology*

Lamivudine in Decompensated Cirrhosis

The clinical course and outcome of Lamivudine therapy in 30 consecutive cirrhotics was analyzed and compared with 30 HBV untreated historical HBeAg-negative controls, matched for age and gender. Significant clinical improvement was defined as a reduction of at least 2 points in the Child-Pugh score and was observed in 23 of 30 treated patients versus none of the 30 patients in the control group after a mean follow-up of 20.6, ±12.1 months. There were ten deaths in the treated group versus 24 in the control group. Liver related deaths occurred in five of the eight patients soon after the development of biochemical breakthrough. Patients with clinical improvement had better survival than patients with no improvement or in those who developed biochemical breakthrough due to YMDD mutants.

It was concluded that Lamivudine significantly improved liver function in HBeAg-negative decompensated cirrhosis. However, the development of the biochemical breakthrough due to YMDD mutants is associated with a fatal outcome. (Manolakoboulos S, Karatapanis F, Elefsiniotis J, et al. "Clinical Course of Lamivudine Monotherapy in Patients With Decompensated Cirrhosis, Due to HBeAg-negative Chronic HBV Infection." *Amer J Gastro,* 2004; Vol. 99, pp. 57–63.)

EUS in Suspected Hilar Cholangiocarcinoma

Prospective evaluation of 48 patients with strictures at the liver hilum were diagnosed by CT and FRCP. All were suspicious of hilar cholangiocarcinoma, but had inconclusive tissue diagnoses. They underwent EUS-FNA with a linear echo endoscope and #22 gauge needles. Adequate material was obtained in 43 of 44 patients. Cytology revealed cholangiocarcinoma in 26 and other malignancies in five. Twelve had benign results. Thirty-two patients underwent surgery. Two had autopsy. Ten were followed up clinically. Four of the benign results were false negatives. No complications occurred. Accuracy, sensitivity and specificity were 91 percent, 89 percent and 100 percent, respectively. EUS and EUS-FNA changed preplanned surgical approach in 27 of 44 patients.

It was concluded that EUS-FNA is of value as a new, less invasive approach for tissue diagnosis in hilar strictures of unknown cause, without significant risks when other diagnostic tests were inconclusive, and was able to change preplanned management in about half of the patients. (Fritscher-Ravens A, Broering DC, Knoefel WT, et al. "EUS-Guided Fine Needle Aspiration of Suspected Hilar Cholangiocarcinoma in Potentially Operable Patients With Negative Brush Cytology." *Amer J Gastro,* 2004; Vol. 99, No. 1, pp. 45–51.)

Infliximab For Perianal Fistulizing Crohn's Disease

Clinical responses and radiologic imaging studies by transperitoneal ultrasound were evaluated in 35 patients with Crohn's disease perianal fistulas after treatment with Infliximab 5mg/kg up to 48 weeks. Follow-up studies at eight weeks and 56 weeks or at discontinuation were assessed by an imaging score of perianal fistula severity, based on Parks criteria. Complete clinical fistula closure and radiologic healing were primary outcome measures.

At eight weeks, after two infusions of Infliximab at 0 and two weeks, clinical fistula closure occurred in 49 percent of patients. The radiologic score at eight weeks was higher for patients with clinical fistula closure than in patients with no clinical improvement, and two patients showed complete radiologic healing. At 56 weeks, clinical fistula closure occurred in 46 percent of patients with correlation between clinical and radiologic scores. There was no association with fistula complexity or the number of fistulas, or the number of collections of baseline imaging.

The proportion of patients with marked radiologic improvement increased from 14 percent at eight weeks to 43 percent at 56 weeks and complete radiologic healing occurred in 11 percent of patients. It was concluded that for perianal fistulizing Crohn's disease, repeat dose Infliximab improves clinical and radiologic outcomes, although complete radiologic healing occurs in a minority of patients. (Rosul I, Wilson SR, MacRae H, Irwin S, Greenberg GR. "Clinical and Radiologic Responses After Infliximab Treatment for Perianal Fistulizing Crohn's Disease." *Amer J Gastro,* 2004; Vol. 99, No. 1, pp. 82–88.)

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