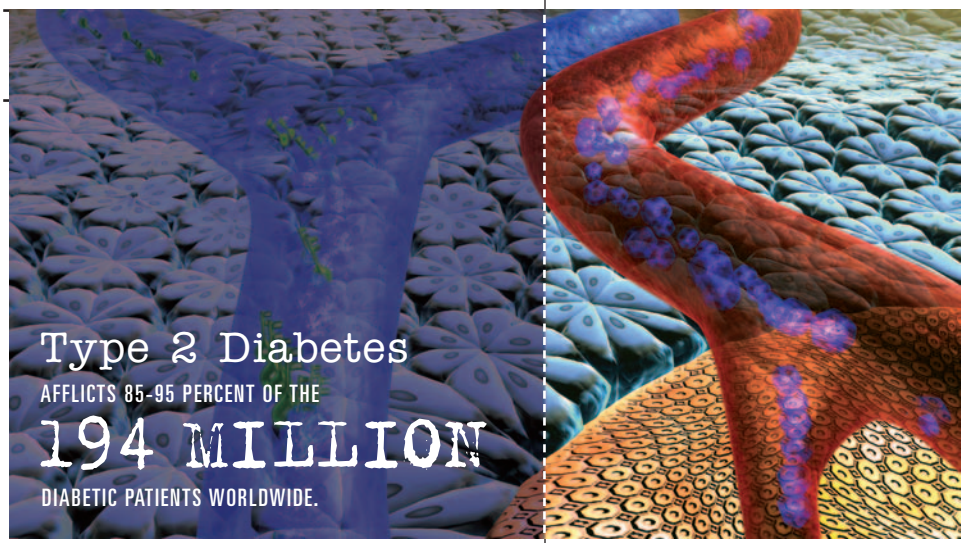
Dear Shareholders:



We are pleased to report on the substantial progress we made in 2006, bringing us closer to reaching our goal of becoming a leading biopharmaceutical company discovering, developing and commercializing innovative therapies for chronic diseases. During the year, we initiated clinical trials for two new product candidates for the treatment of metabolic disease, MB07803, for the treatment of type 2 diabetes, and MB07811, for the treatment of hyperlipidemia (elevated cholesterol and triglycerides). By year-end, enrollment was nearly completed in an important Phase 2b clinical study for CS-917, our first generation product candidate for the treatment of type 2 diabetes, being developed by Daiichi Sankyo. We also completed a promising Phase 1/2 clinical study for MB07133, our liver-targeted product candidate for the treatment of primary liver cancer. Early in 2006, the final results of the successful Phase 2b study for pradefovir, for hepatitis B (HBV), were reported, and by the end of the year we transferred the worldwide rights to the development and commercialization of pradefovir from Valeant Pharmaceuticals International to Schering-Plough. This excellent progress resulted in a total of five product candidates in various stages of clinical trials by the end of the year. In addition, our discovery team had an excellent year, which included the establishment of a collaboration with Idenix Pharmaceuticals, and continued work on the AMPK project with Merck & Co., as well as exciting progress on new metabolic disease projects that could lead to future clinical candidates.

To support all of these efforts, we expanded the Metabasis team in 2006 with key management hires primarily in development, but also in finance and investor relations. In fact, because we are currently independently developing MB07803, MB07811 and MB07133, we doubled the size of our preclinical and clinical development and regulatory teams during 2006. These additions complement an already proven and experienced group. Finally, to support this continued growth and progress, we raised an additional $40 million in capital and established a committed equity financing facility to strengthen our financial resources. Together, these advances set the stage for what we expect will be a productive and exciting 2007.

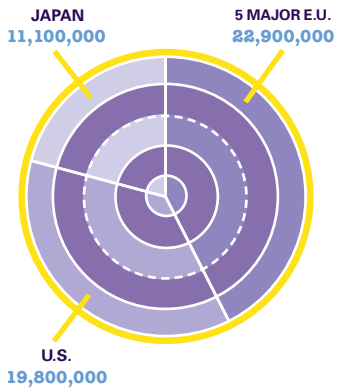
♦♦ PIPELINE PROGRESS:

CS-917

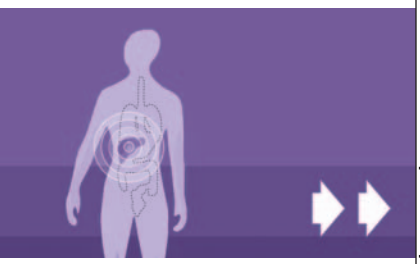
CS-917 represents a new therapeutic approach for the treatment of type 2 diabetes. It is a first-in-class inhibitor of fructose-1,6-bisphosphatase (FBPase), a regulatory enzyme in the pathway responsible for the production of glucose in the liver, known as the gluconeogenesis pathway. Results from preclinical and clinical studies suggest that by specifically inhibiting this pathway, liver glucose production is reduced, resulting in a decrease in blood glucose levels. In February 2006, our partner on the development of CS-917, Daiichi Sankyo, initiated a Phase 2b clinical trial for CS-917, given orally as a single agent to patients with type 2 diabetes. The trial is designed to evaluate the safety and tolerability of CS-917 during three months of dosing, as well as its effect on blood levels of HbA1c, an important measure of long-term glucose control in patients with type 2 diabetes. In January 2007, Daiichi Sankyo informed us that enrollment in the clinical trial was complete with a total of 392 patients having been enrolled in the U.S. If successful, this clinical trial could support selection of a dose for Phase 3 clinical trials.

FACTS: Type 2 Diabetes

- Type 2 diabetes is a leading killer in the U.S., characterized by elevated blood glucose levels resulting from decreased glucose metabolism and increased glucose production.
- Patients with chronically elevated blood glucose levels can develop heart disease, stroke, blindness, kidney disease and nerve damage.



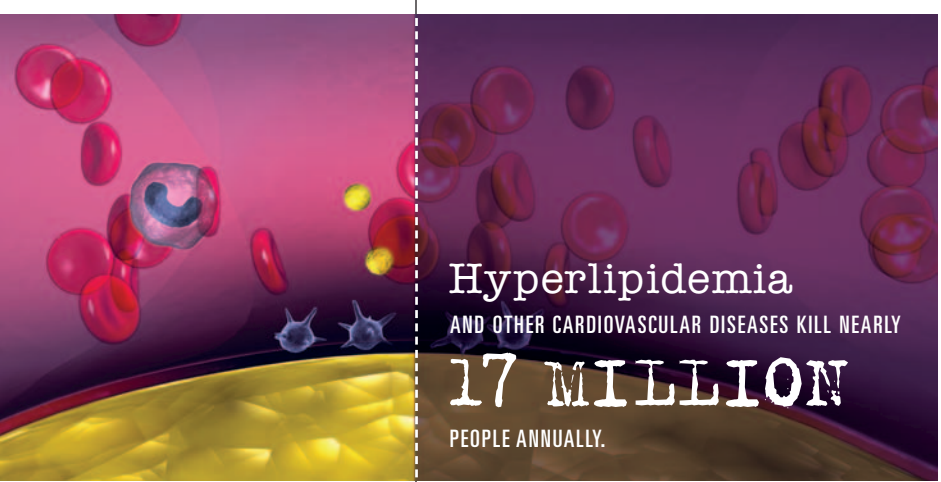
TYPE 2 DIABETES
(WW Prevalence = 207,000,000)

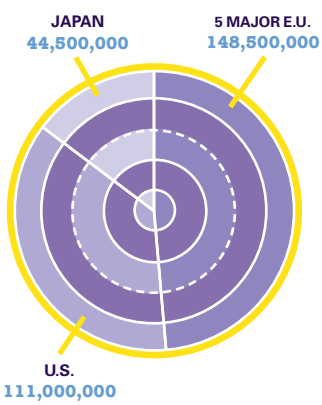


Pipeline Progress (cont'd):

FACTS: Hyperlipidemia

- Over 80% of patients with coronary heart disease remain above the targeted levels for cholesterol and other lipid parameters, increasing risk of heart attack.
- In the U.S. alone, cardiovascular diseases claim more lives than cancer, chronic respiratory disease, accidents and diabetes combined.





HYPERLIPIDEMIA
(WW Prevalence = 301,000,000)

We expect to report top-line results of this study around mid-year.

CS-917 is expected to be used alone or in combination with other diabetes therapies other than metformin. Daiichi Sankyo is funding the development of CS-917 and has worldwide rights to the product candidate, with Metabasis receiving payments upon achievement of certain milestones, royalties on net sales, as well as retaining an option to co-promote the product in North America.

MB07803

The progress on CS-917 increases our confidence in the value of MB07803, our second generation inhibitor of FBPase that we are currently independently developing as a treatment for type 2 diabetes. While MB07803 is structurally different from CS-917, and may offer certain advantages, both agents are designed to inhibit gluconeogenesis by targeting the same binding site on FBPase. We initiated and completed four Phase 1 clinical trials for MB07803 during 2006, another milestone for our metabolic disease product development efforts. The results from the completed clinical trials indicated that MB07803 appears to be safe and well tolerated and, as a result, we initiated a Phase 2a clinical trial for MB07803 for the treatment of type 2 diabetes in the second quarter of 2007.

With the alarming growth in the incidence of type 2 diabetes worldwide, we believe that new treatment approaches are urgently needed. We continue to believe that CS-917 and MB07803 represent an important new therapeutic class of product candidates that have the potential to be an effective approach for treating type 2 diabetes, which is a chronic, life-threatening disease.

MB07811

During 2006, MB07811, our fifth internally discovered product candidate and our third metabolic disease product candidate, entered clinical trials, no small feat for a company at our stage. MB07811 uses our proprietary HepDirect prodrug technology and other structural features to target a beta-subtype-selective thyroid hormone receptor (or TRβ) agonist to the liver to reduce serum cholesterol, specifically the LDL fraction (the "bad" cholesterol) and triglycerides. If liver targeting can unlock the efficacy of the TRβ agonists by avoiding the safety concerns that have prevented them from advancing in clinical development in the past, we may be able to provide physicians and patients with an important new approach to control hyperlipidemia.

We have extensively evaluated the potential of MB07811 in numerous animal models including primates and we are encouraged by the results seen to date. In preclinical animal models, it was shown that MB07811 effectively lowered total serum cholesterol and liver triglycerides. In certain animal models, MB07811 lowered serum cholesterol as effectively as atorvastatin, the active ingredient in the widely-prescribed statin, Lipitor®. MB07811 provided an additive effect in these models when used in combination with atorvastatin and may possibly offer certain other advantages over statins. For instance, our preclinical studies showed a reduction in both serum and liver triglyceride levels, as well as, lipoprotein a [Lp(a)] and, in certain animal models, a reduction in liver fat. High triglycerides and high Lp(a) are lipid measures associated with increased risk of cardiac disease and fatty liver may be associated with increased risk of diabetes and chronic liver disease. Importantly,

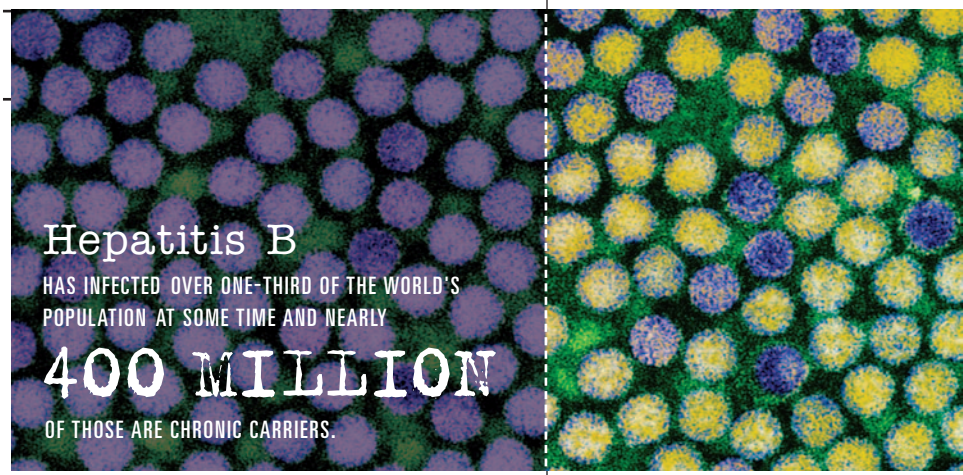
the reductions were seen in these animal models at doses well below doses that are associated with side effects. In other words, MB07811 appears to have a therapeutic index that may be wider than other TRβ agonists tested thus far by other companies. The therapeutic index is the ratio of the dose that causes side effects to the dose that provides the beneficial activity.

In the fourth quarter of 2006, we initiated and successfully completed a Phase 1 clinical trial for MB07811, designed to evaluate its safety and tolerability in a rising single dose study in healthy volunteers. We expect to pursue additional clinical studies of MB07811, including a multiple dose Phase 1b study in healthy volunteers with elevated LDL cholesterol in the second quarter of 2007. This study could provide early evidence of the improved therapeutic index we are seeking by targeting our novel TRβ agonist to the liver.

Pradefovir

At the European Association for the Study of Liver Disease meeting in April 2006, our partner at that time, Valeant Pharmaceuticals International, presented the 48-week results of the completed Phase 2b clinical trial for pradefovir for the treatment of patients with hepatitis B (HBV). The results showed a statistically significant reduction of HBV DNA, a measure of viral load, at the top three doses of pradefovir evaluated in the clinical trial, as compared to the approved treatment for HBV, Hepsera™, administered at its maximum allowable dose. Both pradefovir and Hepsera are prodrugs of the anti-viral drug adefovir; however, only pradefovir uses the HepDirect liver-targeting technology. In the Phase 2b studies, pradefovir treatment, even at the highest dose tested, resulted in lower circulating levels of adefovir than did Hepsera administered at its maximum approved dose. This finding is consistent with expectations for the HepDirect prodrug technology and important because high circulating levels of adefovir may lead to renal toxicity. In fact, Hepsera is dose-limited due to renal toxicity observed at high doses.

Until the end of 2006, pradefovir had been developed through a collaboration with Valeant. In December 2006, Metabasis and Valeant agreed to license and assign Valeant's development and commercial rights to pradefovir to Schering-Plough, a company with a global reach and a long-standing commitment to the development and commercialization of products for the treatment of hepatitis.



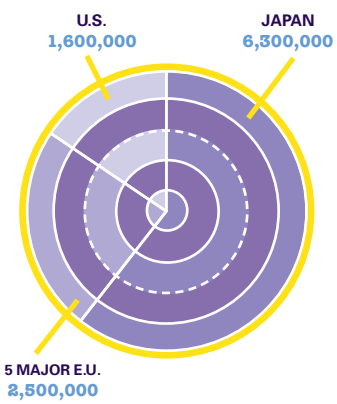
MB07133

MB07133 is in clinical development for the treatment of primary liver cancer, a deadly disease for which there are currently no FDA-approved drug therapies. MB07133 uses our HepDirect technology to target an activated form of the leukemia drug, cytarabine, to the liver, while decreasing levels in tissues outside of the liver. We believe that by directly delivering an activated form of cytarabine to the liver, we can effectively target the tumor cells while potentially reducing or avoiding extra-hepatic side effects such as bone marrow suppression and gastrointestinal side effects.

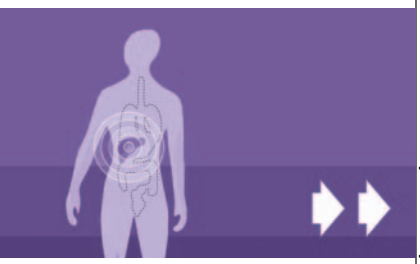
We completed a Phase 1/2 dose escalation clinical trial for MB07133 in 28 patients by the end of the year and preliminary results were presented at the 2006 American Society of Clinical Oncology meeting. Results of the clinical trial indicated that MB07133 at doses up to 2400 mg/m2/day IV infusion was well tolerated in patients with primary liver cancer and that there were no clinically significant dose-limiting toxicities associated with MB07133. Although this Phase 1/2 clinical trial was not designed to demonstrate the efficacy of MB07133, encouraging signs of drug activity were observed, including evidence of disease stabilization and tumor shrinkage in some patients who received multiple cycles of the product candidate. These results are considered promising, given the usual deadly progression of primary liver cancer.

FACTS: Hepatitis B

- Hepatitis B is the most common serious liver infection in the world.
- It can lead to complications such as cirrhosis, primary liver cancer and potentially death.
- Approximately 1.2 million deaths worldwide are hepatitis B-related.



HEPATITIS B
(WW Prevalence = 400,000,000)



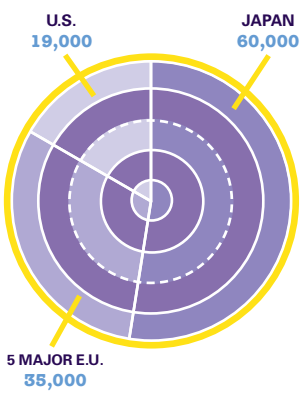
Pipeline Progress (cont'd):

FACTS: Primary Liver Cancer

- There are currently no FDA-approved therapies or standards of care and few treatment options available for patients with primary liver cancer.
- The median survival time for patients with primary liver cancer from point of diagnosis is four–six months.

The next clinical trial for MB07133 is expected to start after discussions with the FDA regarding the future development of the product candidate, likely later in 2007.

DISCOVERY PROGRAMS:
Finally, we continue to form collaborations that further leverage our proprietary technologies, scientific expertise and unique capabilities in targeting the liver and liver pathways. In the fourth quarter of 2006, we entered into a two-year research collaboration agreement with Idenix. Under the terms of the agreement, Metabasis' HepDirect liver-targeting technology will be applied to proprietary Idenix compounds with the goal of developing second-generation nucleoside analog clinical candidates for the treatment of hepatitis C virus. This is similar to an earlier collaboration we had formed with Merck & Co. The collaboration with Idenix could provide us with as much as $68 million upon reaching certain preclinical and clinical milestones and regulatory approvals. We also continued to work on a second collaboration with Merck & Co. to discover and, if successful, develop and commercialize novel small molecule therapeutics with the potential to treat several metabolic diseases, including type 2 diabetes, hyperlipidemia and possibly obesity by activation of an enzyme in the liver called AMP-activated Protein Kinase (AMPK).



PRIMARY LIVER CANCER
(WW Prevalence = 625,000)

A TARGETED APPROACH FOR SUCCESS:
To date, we have internally discovered all of our product candidates and have built a pipeline rich with potential opportunities for growth. We started last year with three product candidates in clinical development, one of which we were developing independently. At year-end, we had five product candidates in clinical development, with three being independently developed. The progress we made during 2006 in advancing all five of these clinical-stage programs puts us within reach of several important, potentially value-building milestones in 2007. In 2007, we expect to advance all the current clinical programs, and most especially have a breakout year for our metabolic franchise while, at the same time, our research team continues to seek new clinical candidates in this area. We expect that research and development progress during 2007 will build value for our shareholders and bring us closer to our goal of establishing Metabasis as a leading biopharmaceutical company discovering, developing and commercializing innovative therapies to treat major chronic diseases.

We thank our employees, partners and shareholders for their dedication and support during 2006 and look forward to a very exciting 2007.

Paul K. Laikind, Ph.D.
President and
Chief Executive Officer

David F. Hale
Chairman,
Board of Directors