2007 ANNUAL REPORT

metabasis

OUR PRODUCT PIPELINE

CORE PRODUCT CANDIDATES: METABOLIC DISEASES

PRODUCT CANDIDATES	DISEASE/ CONDITION	MECHANISM	PARTNER	OUR COMMERCIAL RIGHTS	PIPELINE STATUS
MB07803	Diabetes	FBPase Inhibitor	None	Worldwide	Phase 2a
MB07811	Hyperlipidemia	TRβ Agonist	None	Worldwide	Phase 1b
Undisclosed	Diabetes	Glucagon Antagonist	None	Worldwide	Preclinical
Undisclosed	Hyperlipidemia	TRβ Agonist	None	Worldwide	Preclinical
Undisclosed	Diabetes/ Hyperlipidemia	AMPK	Merck	Royalties, North America U.S. Co-promotion Option	Preclinical

NON-CORE PRODUCT CANDIDATES: LIVER DISEASES

PRODUCT CANDIDATES	DISEASE/ CONDITION	MECHANISM	PARTNER	OUR COMMERCIAL RIGHTS	PIPELINE STATUS
MB07133	Primary Liver Cancer	Prodrug of activated cytarabine	None	Worldwide	Phase 1/2 Completed
Pradefovir	Hepatitis B	Prodrug of adefovir	None	Worldwide	Phase 2b Completed
Undisclosed[1]	Hepatitis C	Undisclosed	Merck/Idenix	Royalties	Discovery

(1) Metabasis' liver targeting technology applied to partners' candidate compounds.

METABASIS is a biopharmaceutical company using its proprietary technologies, scientific expertise and unique capabilities for targeting the liver and liver pathways. The Company has established a broad pipeline of product candidates and advanced research programs targeting large markets with significant unmet needs. Metabasis' core area of focus is on the discovery and development of drug candidates to treat metabolic diseases such as hyperlipidemia and diabetes, among others. Although not a core focus of the Company, Metabasis has also discovered and developed drug candidates indicated for the treatment of liver diseases such as hepatitis and primary liver cancer, which it now intends to license or partner. All product candidates were developed internally using proprietary technologies.

DEAR SHAREHOLDERS

Focusing On Our Strengths And Opportunities

Since our inception, our goal has been to grow into a leading bio-pharmaceutical company that develops, discovers and commercializes innovative therapies to treat chronic diseases. Of course, the path to such an important goal is never without challenges and our decision in 2007 to discontinue development of CS-917, our first-generation FBPase inhibitor for the treatment of type 2 diabetes, was a significant setback. However, we adjusted our strategy and made excellent progress during the year, advancing our second-generation FBPase inhibitor, MB07803, into a key Phase 2 clinical trial and reporting promising preliminary results from a Phase 1 clinical trial for our novel treatment for hyperlipidemia, MB07811. We believe that this progress has positioned us for a very exciting 2008, with important clinical trial data expected from both these key programs. If all goes according to plan, we also expect to recommend the development of new product candidates for treating metabolic disease, and to announce important strategic collaborations.

For a number of years, our internal efforts have been primarily focused on discovering and developing important new treatments for metabolic disease, and the revised strategic plan we announced in 2007 confirmed that focus. This strategy includes advancing our clinical stage "core" metabolic disease assets through key milestones, while also expanding our pipeline of product candidates. As previously mentioned, we made significant clinical progress in 2007 with our two leading product candidates, MB07803 and MB07811, both of which we are currently developing independently. Additionally, over the next few years, we intend to expand our existing pipeline of core assets by moving promising metabolic disease product candidates from research and preclinical development into clinical development. Two such programs, from which we expect to recommend product candidates for development in 2008, are our orally bioavailable glucagon antagonists for the treatment of type 2 diabetes and our second-generation liver-targeted TRß agonists for treating hyperlipidemia. We also continue to collaborate with Merck & Co. on the development of activators of an enzyme known as AMP-activated Protein Kinase (AMPK) for treating type 2 diabetes and potentially other metabolic diseases.

type 2 diabetes market[1]

US PATIENTS: 18 MILLION PEOPLE

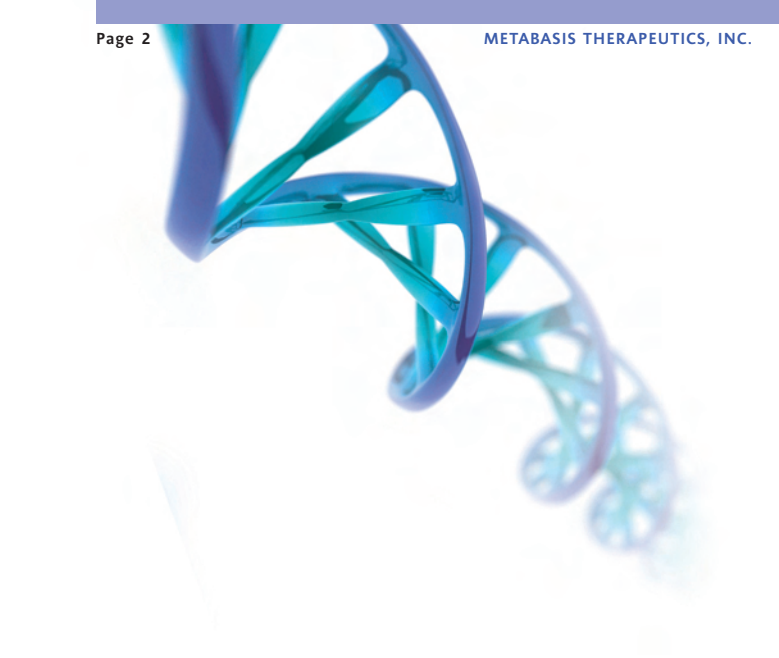
US SALES: $11 BILLION

US COSTS: $174 BILLION

Worldwide in 2007, there were an estimated **246 million patients** suffering with type 2 diabetes, with sales of products exceeding **$17 billion**. Estimated healthcare costs associated with type 2 diabetes were at least **$232 billion** in 2007.

Another important element of our revised strategic plan involves establishing strategic collaborations designed to maximize the current and future value of our assets. In the area of metabolic disease, strategic collaborations are critical for assuring a comprehensive development and commercialization program. Given the potential of the novel and significant targets that we are pursuing, we believe we have an excellent opportunity to establish important collaborations that will allow us to accelerate the development of our product candidates, participate in future clinical development and commercialization and build value for our shareholders. Potential collaborators have already shown significant interest in each of our core product candidates as well as our "non-core" liver disease product candidates.

With respect to our non-core assets, our intention is to further enhance the value of these clinical stage candidates by licensing them for future clinical development and commercialization or otherwise selling them to provide near term resources to reinvest in our core business. Our non-core product candidates include MB07133, for the treatment of primary liver cancer, and pradefovir, for the treatment of hepatitis B.



Our product candidates hold the potential to help patients with some of the world's most devastating and prevalent diseases. If successful, each of our product candidates could represent important new therapeutic approaches in one of the world's largest and fastest growing pharmaceutical market segments. Because of this, we believe that successful clinical development of our product candidates would create significant value for our shareholders. We feel that the implementation and evolution of our strategic plan has set the stage for a productive and eventful 2008 and beyond.

Focusing On Our Core Pipeline Progress

MB07803 is a second-generation product candidate for the treatment of type 2 diabetes, and part of a new class of drugs that Metabasis discovered internally using our NuMimetic™ technology. MB07803 is designed to regulate glucose production in the liver by inhibiting an enzyme known as fructose-1,6-bisphosphatase (FBPase), a key component of the gluconeogenesis pathway. MB07803 was selected for clinical development based on preclinical studies showing it to have a more favorable pharmacokinetic profile and enhanced potency compared to the first-generation compound, CS-917, also discovered by Metabasis, but discontinued in 2007 in favor of MB07803. The improvements include once-a-day dosing, increased bioavailability, and reduced metabolism and variability. The results seen thus far in multiple completed Phase 1 clinical trials are consistent with these findings.

We recently completed a Phase 2a proof-of-concept clinical trial for MB07803, which was a randomized, double-blind, placebo-controlled, 28-day clinical trial involving over 100 patients with type 2 diabetes. One group received a placebo, and the other four groups received different doses of MB07803, administered once daily. The clinical trial evaluated the change from baseline in fasting plasma glucose levels of MB07803-treated patients relative to placebo-treated patients. Results from this clinical trial may provide evidence for the strong potential of MB07803 as an important new approach for treating patients with diabetes with an improved profile relative to CS-917. We expect to initiate and complete an important clinical trial later in 2008 that could provide initial evidence that there are no safety concerns when MB07803 is co-administered with metformin, a widely used product for the treatment of patients with type 2 diabetes. We also believe that the results from the key clinical trials conducted in 2008, if successful, will support the establishment of a strategic collaboration for MB07803, as well as provide the information needed to launch a Phase 2b clinical trial with three-month dosing.

MB07811 is a novel, orally active product candidate for the management of hyperlipidemia, discovered internally by Metabasis. MB07811 uses the Company's proprietary HepDirect® prodrug technology to target a novel beta-subtype-selective thyroid hormone receptor (TRß) agonist to the liver to reduce fat protein complexes called lipoproteins including low density lipoprotein, or LDL-cholesterol (LDL), serum triglycerides (TGs), liver triglycerides (which may lead to unhealthy liver fat accumulations) and Lp(a), a lipoprotein potentially associated with coronary artery disease. High levels of cholesterol and triglycerides are associated with an increased risk of cardiac disease, and fatty liver is associated with increased risk of diabetes and chronic liver disease. Numerous studies have shown that lowering LDL in particular is associated with improved outcomes in cardiovascular disease.

Thyroid hormone receptor (TR) agonists represent a novel and potentially important approach for treating hyperlipidemia. The

potential efficacy of this approach has been demonstrated in both preclinical and clinical trials; however, use of this approach has been hampered by side effects associated with thyroid hormone, including cardiac effects and effects on the thyroid hormone axis, muscle metabolism and bone turnover. We believe that liver targeting may avoid the safety concerns previously seen with other TRß agonists, thus unlocking the therapeutic potential of this approach.

MB07811 is designed to deliver a novel TRß agonist to the site where cholesterol is produced and metabolized, i.e. the liver, while reducing the exposure of the agonist to other tissues. This last point is important — getting a TRß receptor agonist to the liver is a significant first step. However, it is equally important to ensure that any active agonist that escapes the liver is unable to be taken up by other tissues. As discussed in a paper published in the *Proceedings of the National Academy of Sciences* (PNAS) in 2007, the combination of our proprietary HepDirect technology and features we have built into the structure of the compound itself, is designed to accomplish these goals.

Preclinical studies demonstrated that MB07811 significantly lowers LDL and total cholesterol and TG levels and, in certain animal

models, reduces liver fat content — all with a significantly improved safety profile relative to non-liver-targeted TRß agonists. Oral administration of MB07811 in a primate model led to cholesterol-lowering activity comparable to Lipitor® (atorvastatin), which is the most widely used drug for the treatment of patients with high cholesterol. In the same model, MB07811 was shown to provide an additive benefit when administered in combination with this widely used statin. These findings were presented by Metabasis in 2007 at scientific conferences, as well as in the above-mentioned PNAS publication.

In addition to this preclinical work, we successfully completed a rising single dose, Phase 1a clinical trial for MB07811 in healthy volunteers in 2006. We initiated a rising multiple dose Phase 1b clinical trial in the second quarter of 2007, designed to evaluate the safety and tolerability of MB07811 in healthy volunteers with modestly elevated cholesterol. The purpose of this clinical trial is to determine a range of doses at which MB07811 can be administered without evoking a therapy-limiting side effect — the broader this dose range is, the better chance we have of demonstrating a wide therapeutic index. This will allow us to select the doses for further study and also help us to understand the potential therapeutic index for MB07811.

Early in 2008, we announced preliminary results from the ongoing Phase 1b clinical trial that indicated MB07811 was safe and well tolerated at the first four dose cohorts; each cohort included eight volunteers, two on placebo and six who received MB07811. We also evaluated the efficacy of MB07811 at the four doses studied. While these observations should be considered preliminary, the results were encouraging, with clinically-relevant reductions in LDL and TGs observed relative to the changes seen in patients treated with placebo.

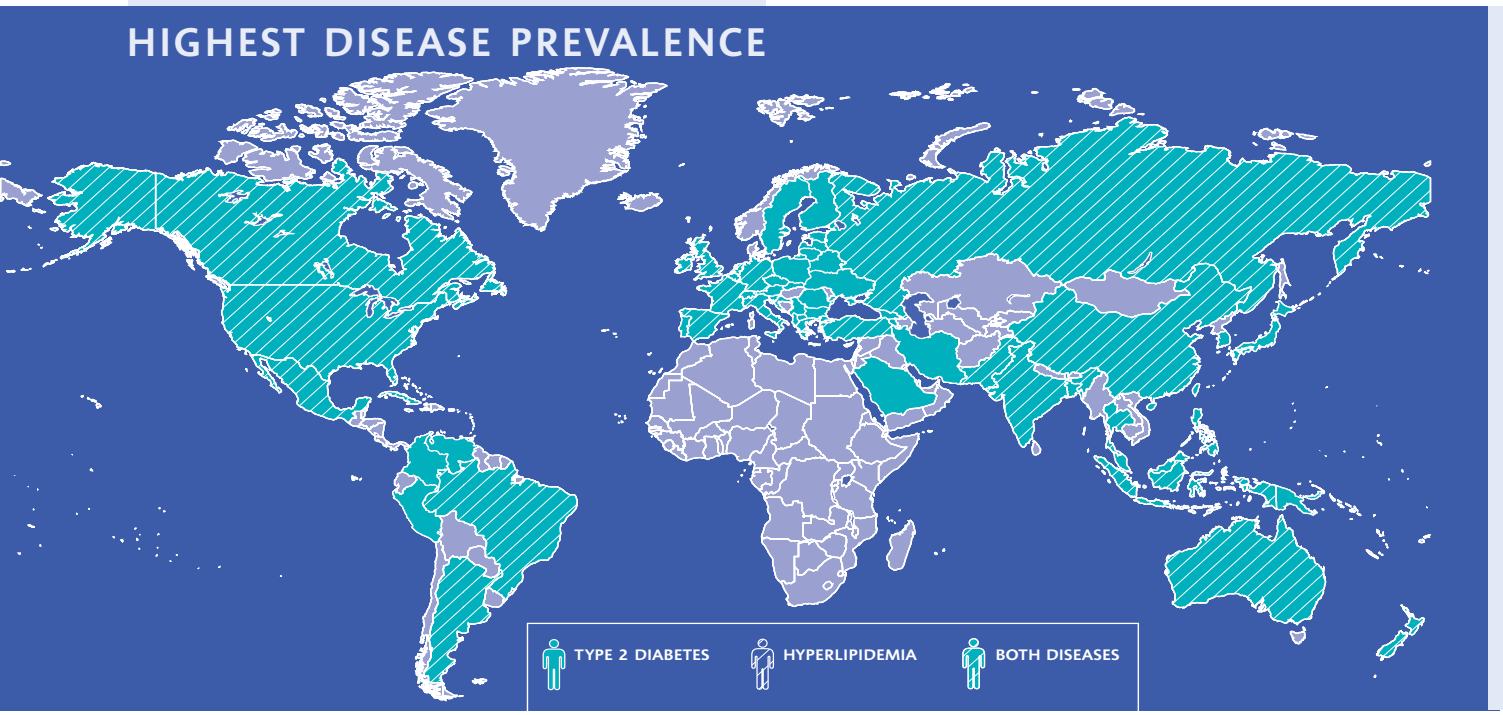
Based on findings showing the first four doses to be safe and well tolerated, we were able to initiate and have now completed a fifth, sixth and seventh and final dose cohort. We expect to report final results from this clinical trial in the second quarter of 2008. In the meantime, we are preparing to initiate an important 12-week, Phase 2a proof-of-concept clinical trial for MB07811, also at mid-year. And, before the end of 2008, we expect to complete an important drug-drug interaction clinical trial to evaluate the safety of MB07811 when combined with a statin. If approved, MB07811 could be an important new approach which may help patients better reach targeted lipid levels while also providing additional benefits.

Cutting Edge Discovery Programs

The same talented team that discovered each of our product candidates currently in clinical development is now working to add exciting new candidates to our pipeline. Several metabolic disease projects are approaching the point where we may be able to recommend candidates for clinical development, and we expect that additional product candidates could be added to our pipeline in 2008.

The first program expected to be recommended is a glucagon antagonist for treating patients with type 2 diabetes. Glucagon opposes the activity of insulin leading to an inappropriate increase in glucose production by the liver and other metabolic disturbances in patients with type 2 diabetes. We have an advanced research program that is focused on identifying chemically novel, potent, orally bioavailable glucagon antagonists. Our most advanced compound has shown significant and consistent lowering of blood glucose when dosed orally in numerous diabetic animal models. Finding an effective, orally active glucagon antagonist has been a goal for many companies, thus our work has attracted the attention of a number of pharmaceutical companies. We have opened discussions with many of these companies as we actively seek a strategic collaborator to help us maximize the benefits of our work in this area and to further support our efforts to provide patients and physicians with new medicines to treat metabolic diseases.

We also have an advanced research program to identify second-generation TRß agonists for treating hyperlipidemia. This program may yield additional development candidates that lower cholesterol and triglycerides by the same mechanism as MB07811, but with potential improvements.



Finally, we have an advanced research program, being conducted in collaboration with Merck & Co., which is focused on identifying drug candidates that activate AMPK to treat type 2 diabetes and potentially other metabolic diseases. This program may yield development candidates as early as 2009 to further expand our product pipeline. In addition, our discovery team continues to work on several research programs beyond these that could yield future potential product candidates.

Non-Core Liver Product Candidates

As previously mentioned, we are focusing the majority of our internal resources on our core metabolic disease assets. However, we remain enthusiastic about the potential of our non-core, liver disease product candidates, MB07133 and pradefovir. Our objective is to license both product candidates.

We successfully completed a Phase 1/2 clinical trial for MB07133, designed to evaluate its safety and preliminary efficacy in patients with inoperable primary liver cancer. Last year, we received Orphan Drug Designation from both the FDA and the European Commission for MB07133 and we are finalizing plans for the next step in the clinical development of this product candidate. We are planning to license MB07133 and to have the next clinical trial, likely a combination trial with Nexavar® (sorafenib), to be initiated by the licensee. Licensing discussions for MB07133 are underway.

Pradefovir is the product candidate for the treatment of hepatitis B that successfully completed a Phase 2b clinical trial. This product candidate was licensed to Schering-Plough Corporation, and as previously reported, Schering-Plough elected not to proceed with the development of pradefovir and has now returned all rights and related assets to us. At this time, we do not intend to independently develop pradefovir, but expect to license this product candidate for further development and commercialization pending the final evaluation of the data returned to us from Schering-Plough.

hyperlipidemia market[2]

US PATIENTS: 111 MILLION PEOPLE

US SALES: $22 BILLION

US COSTS: $400 BILLION

In 2006, in the seven major markets,[3] there were an estimated **301 million patients** suffering from hyperlipidemia, with sales of products to treat the disease exceeding **$30 billion**.

Focusing On Our Future

The progress we have made to advance our clinical stage pipeline, as well as our ongoing discovery efforts, puts us in reach of several important milestones in 2008 and beyond. Pipeline progress and growth, results from key clinical trials and expected strategic collaborations all represent important, potentially value-driving events that should make 2008 an exciting year for Metabasis and our shareholders. It is no small feat for a company of our size and age to have put multiple important product candidates into clinical development with more on the horizon. We are very proud of the fact that with our proprietary technologies, we have internally discovered and continue to discover numerous innovative new ideas for treating chronic worldwide diseases. We thank our committed and hard working employees and our shareholders for their support during 2007 and look forward to sharing our progress in 2008.

Paul K. Laikind, Ph.D.
PRESIDENT AND CHIEF EXECUTIVE OFFICER

David F. Hale
CHAIRMAN, BOARD OF DIRECTORS