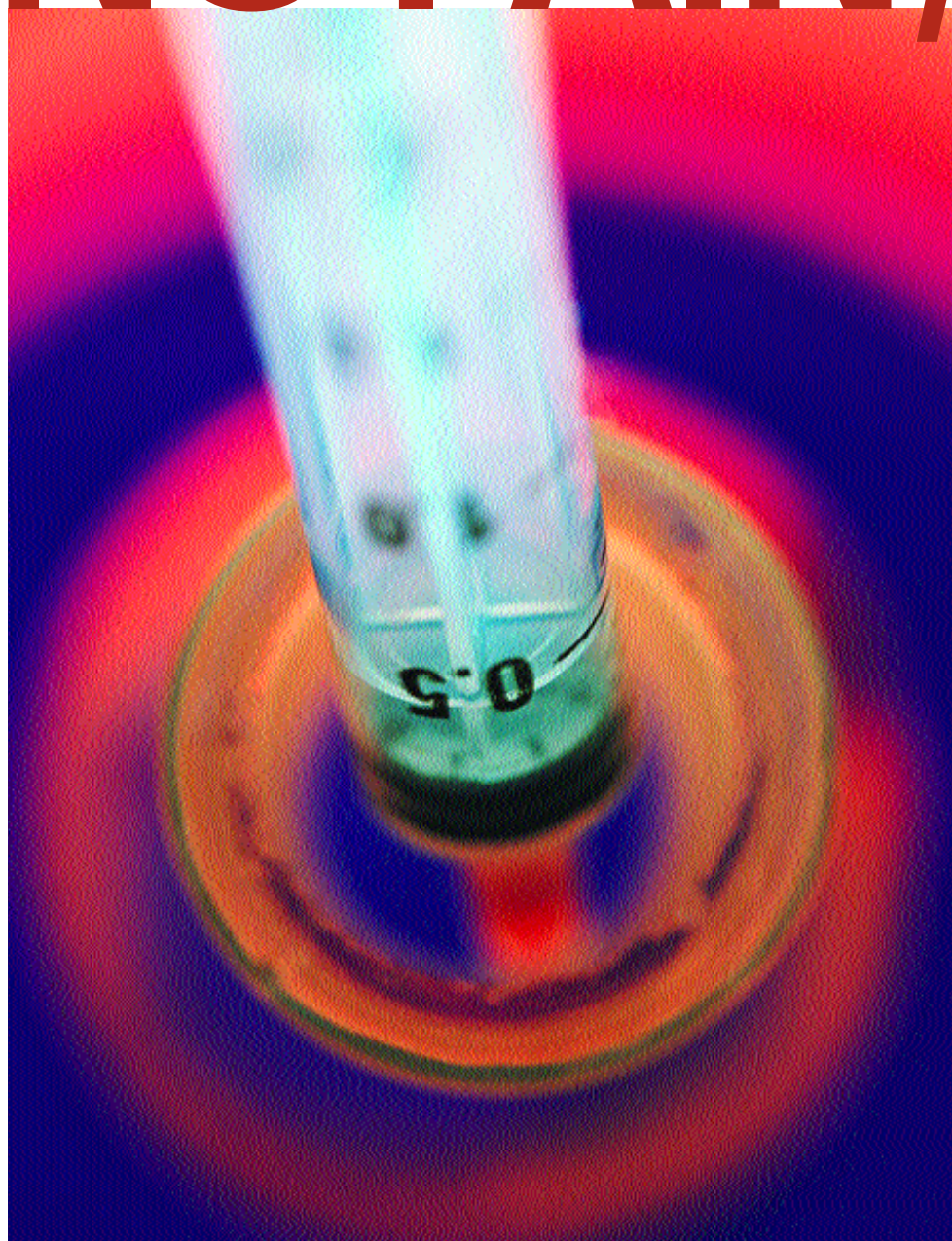


# NO PAIN,



# BIG GAIN

The company that can bring to market the first safe and effective non-injectable method of insulin delivery may reap great rewards

**D**aily injections are a painful way of life for an estimated 3.7 million Americans who are insulin-dependent diabetics. The condition, characterized by high blood sugar levels that result from defects in the body's ability to produce and/or use insulin, is the fifth leading cause of death by disease in the U.S., and can lead to severely debilitating or fatal complications, such as blindness, kidney disease, heart disease, and amputations.

Current treatments are effective in controlling the disease, but patient compliance is a very real concern because the available insulin delivery technologies are invasive and cause fear and pain. Most diabetic patients need to inject insulin multiple times in a day, which adds to the trauma. Pharmaceutical companies continue to work toward finding a way to improve insulin delivery, despite obstacles and past failures.

"Everybody is trying to be the first to introduce an alternative insulin delivery for the simple reason that there are millions of patients who depend on insulin every day and they are really tired of using needles," says Ajit Baid, pharmaceutical industry analyst at Frost & Sullivan.

There is no question that there is an unfulfilled need in the diabetes treatment market for an alternative to insulin injections. Besides the discomfort of insulin injections, side effects include hypoglycemia (low-blood sugar), hyperglycemia (high-blood sugar), and potential injection-site infections.

“Within the insulin field today, all the major pharmaceutical companies have expressed significant interest in non-injectable insulin because they all realize how important the unserved need is in diabetes and the tremendous growth opportunity that exists,” says Michael Goldberg, M.D., Chairman and CEO of Emisphere Technologies.

The alternative insulin delivery methods being developed include inhalable, oral, patch, and oral spray delivery systems. Of the products currently in development, none will address all the insulin needs of the type 1 diabetic, who is completely insulin dependent and requires at least three to four injections daily, including long-acting and mealtime insulin.

Where these delivery methods could be of benefit to type 1 diabetics is in reducing the amount of injections needed, since the products in development may be used in conjunction with injectable insulin.

The benefits for type 2 diabetics, the majority of the nation’s approximately 17 million diabetes sufferers, are even greater. The needle-free products in development may eliminate the need for patients to ever use an injectable insulin product in the future. The option to use insulin without injections may improve compliance among type 2 diabetics.

“Type 1 diabetics are reliant on insulin because they don’t produce the hormone, so these patients are more compliant,” Mr. Baid says. “However, type 2 diabetics may either have inadequate insulin production or may be insulin resistant and their bodies are still coping, so they are relatively less compliant. Some of the reasons for non-compliance are the pain, fear, and embarrassment associated with needles. Non-injectable insulin should help address the compliance issue.”

Further compounding poor compliance is that type 2 diabetics typically are older patients who do not want to deal with daily injections.

“Shots are particularly a barrier for older people with type 2 diabetes,” says Francine Ratner Kaufman, M.D., professor of pediatrics, Childrens Hospital Los Angeles, and president of the American Diabetes Association.

Developers of needle-free products believe that more desirable methods of insulin treatment will open the door for type 2 diabetics, who are using insulin therapy.

“By providing a noninvasive way to give insulin, we will be able to offer another option to people who have resisted insulin therapy because of their fear of needles,” says Mads Krogsgaard Thomsen, D.V.M., Ph.D, D.Sc., chief science officer of Novo Nordisk AS. “These individuals suddenly will have a chance to get their diabetes in control, which may reduce the risk of complications, such as blindness, amputations, and dialysis.”

But specialists warn there are other issues to consider. “Obviously any kind of new innovation reinvigorates people to stick to the regimen, so non-injectable insulin will have some advantages, but it will certainly not be the ultimate answer since insulin, given by any means, is not the cure for diabetes,” Dr. Kaufman says.

Needle-phobia is not only a problem with patient compliance, but also with a doctor’s willingness to initiate insulin treatment in type 2 diabetics.

“For a drug that’s been around since 1922, there is a lot of reluctance on the doctors’ part to prescribe insulin,” says Evan D. Rosen, M.D., Ph.D., assistant professor of medicine at Harvard Medical School, assistant professor of medicine at Beth Israel Deaconess Medical Center, and diabetes medical director at Veritas Medicine. “Many physicians don’t really understand how to tell people to administer injectable drugs. In addition, there is equipment that goes along with it — glucometers, alcohol swabs, finger sticks, and test strips — all of this is confusing for doctors who don’t have a team of nurse educators to help patients do what is needed.”

## CHANGING THE APPROACH TO TREATMENT

In addition to improvements in patient comfort and compliance, alternative insulin delivery methods may change the way type 2 diabetes is treated, possibly improving the health of those with the disease.



IF THE SAFETY AND EFFICACY OF ORAL INSULIN CAN BE ESTABLISHED THERE IS NO DOUBT THAT IT WILL BE THE MOST SUCCESSFUL INSULIN DELIVERY METHOD.

**AJIT BAID**





**WE THINK THE MARKET IS LARGE ENOUGH THAT CERTAINLY MORE THAN ONE PRODUCT CAN BE ACCOMMODATED, HOWEVER, WE BELIEVE THAT BEING FIRST TO MARKET WILL BE VERY IMPORTANT FOR ORAL INSULIN.**

**DR. CHRISTOPHER PRICE**

Currently, treatment for type 2 diabetes begins with adjustments in diet and exercise. If blood glucose cannot be regulated with diet and exercise, treatment is initiated with oral hypoglycemic agents or oral antidiabetic agents, such as sulphonylureas, prandial glucose regulators, biguanides, insulin sensitizers, and alpha-glucosidase inhibitors. As type 2 diabetes progresses, tablets can become ineffective in maintaining the appropriate blood glucose levels and insulin is used to keep diabetes in control.

Developers of non-injectable insulin believe the needle has been a barrier to the early treatment of type 2 diabetes with insulin. Needle-free products could change insulin treatment for individuals with type 2 diabetes from a final option to a first-

line of action.

By introducing insulin therapy earlier in the type 2 diabetic's disease progression, some researchers believe that pancreas function can be preserved, since it is the islet cells within the pancreas that secrete insulin. This also would lessen the side effects of the disease.

"Some of the thinking now is if patients with type 2 diabetes could begin insulin therapy earlier this can reduce the stress on the islet cells and allow some recovery reducing the chances of a bad pathology," says Jonathan Eppstein, president of research and chief technical officer of Altea Development Corp.

"The real opportunity here is to begin early in the type 2 disease state and prevent progression of the disease," Dr. Goldberg says. "In the case of type 2 diabetes, in contrast to type 1 diabetes, the condition is initially a disease of the end organs, it is not a disease of the pancreas, which produces insulin."

Often because of a fear of needles and using insulin, type 2 diabetes patients who would benefit from early insulin treatment compromise their long-term health by delaying adding insulin to their therapeutic regimen.

"In my practice, I often have first-time patients come in who are on three or four oral medications when they really ought to be on insulin," Dr. Rosen says. "There are a lot of type 2 diabetics with poorly controlled diabetes because they are afraid of using insulin; if they had a less intimidating option for controlling their disease they would be more likely to use insulin."

## DEFINING THE MARKET

Despite excitement about advances in new insulin delivery technologies, analysts do not expect all diabetics to switch right away to non-injectable insulin. Newly diagnosed diabetics are expected to make up the majority of the first patients to use these products, followed by existing diabetics.

"Inhalable insulin is likely to come to the market well before the other forms of non-injectable insulin," Mr. Baid says. "In the first two years these products won't really expand the market. I would estimate that 3% to 4% of patients will shift to inhalable insulin during the first year of introduction, which will eventually increase to 7% and 8% in the following year."

Part of the slow uptake for such a revolutionary treatment is expected to be physicians' concerns about safety and dosing.

"Among diabetes doctors there is going to be a bit of reluctance initially," Dr. Rosen says. "There is concern that if it becomes easier to take insulin, then patients could over-treat themselves. Patients won't recognize that there is a lag between the administration and the time it takes insulin to work. Patients may take a dose, check their blood sugar an hour later and if it is not down enough, redose, which can lead to a crash in blood sugar. This is not the case with injectable insulin as patients don't like to keep injecting themselves. That doesn't mean we shouldn't proceed in this direction, it just means we need to be vigilant about warning people about these potential problems."

Dr. Rosen believes that the marketers of these products are going to have to present their products with standardized dosing, so that doctors can relate them to the insulin dosing that they are accustomed to with injectable insulin.

"If I give somebody an injection of 15 units of insulin, I know exactly what is going to happen, but if I have someone take two puffs, I don't really know what's going to happen," Dr. Rosen says. "There is going to be an initial reluctance by some doctors to make that leap. There is going to have to be a standardization of dosing."

Analysts agree that as with any new form of treatment, safety will be one of the major concerns for all the non-injectable insulin products in development.

“The first challenge is to finally get a product which is as efficacious as the traditional insulin technologies, like insulin syringes, pens, injectors, and pumps,” Mr. Baid says. “The second challenge is that it has to be safe. Safety is very, very important and physicians are going to watch before they start prescribing.”

Dr. Rosen adds, however, “As a practicing diabetologist I welcome another form of insulin. The best benefit will be getting people on board who otherwise won’t even listen when I suggest taking injectable insulin. I am very excited about that possibility, and leery of the safety issues; we’ll just have to see how it plays out.”

## BREATHING EASY

Of the needle-free delivery systems in development, the most advanced are two inhalable insulin products in Phase III trials. Pulmonary insulin is expected to be the first needle-free insulin to be marketed in the U.S., with an estimated launch by 2004 or 2005.

The most advanced pulmonary insulin product is Exubera, which is being developed through a global co-development, co-promotion, and co-manufacturing collaboration between Pfizer Inc. and Aventis Pharma. Pfizer also is in a collaboration with Inhale Therapeutic Systems Inc., developers of Exubera’s inhalation device and formulation process.

## The Future of Insulin: Selected Products in Development

### INHALED INSULIN

#### PHASE III

**Exubera** (Pfizer Inc. and Aventis Pharma)  
**NN1998** (Aradigm Corp. and Novo Nordisk)

#### PHASE II

**Aerodose** (Aerogen Inc.)

#### PHASE I

**AIR** (Alkermes and Eli Lilly & Co.)

#### PRECLINICAL

**Bio-Air** (BioSante Pharmaceuticals Inc.)

### ORAL INSULIN

#### PHASE I/II

**Hexyl-Insulin Monoconjugate (pill)** (Nobex Corp. and GlaxoSmithKline)  
**Insulin (capsule)** (Emisphere Technologies)

#### PRECLINICAL

**Capic (calcium phosphate delivery system)** (BioSante Pharmaceuticals Inc.)

### TRANSDERMAL INSULIN

#### PHASE I/II

**MicroPor (skin patch system)** (Altea Development Corp.)

### NASO-PULMONARY INSULIN

#### UNDISCLOSED

**Oralin oral spray** (Generex Biotechnology Corp.)



WE ARE DELIVERING INSULIN, REGULAR RECOMBINANT HUMAN INSULIN; THE MAIN DIFFERENCE IS THAT WE’RE GIVING IT AT A CONTROLLED BASAL RATE WITH A 24-HOUR PATCH. ANY PERSON WITH DIABETES WHO COULD BENEFIT FROM BASAL INSULIN DOSING WOULD BE A POSSIBLE CANDIDATE.

**JONATHAN EPPSTEIN**

## Diabetes Market Facts

- **AMERICANS WITH DIABETES:** **17 million**, 6.2% of the population — 11.1 million are diagnosed, 5.9 million are undiagnosed
- **DIABETES BREAKDOWN:** Type 1 diabetes prevalence **5% to 10%**, type 2 diabetes prevalence **90% to 95%**
- **PREVALENCE AMONG CHILDREN:** About **one in every 400 to 500 children** and adolescents has type 1 diabetes. About 151,000 people younger than 20 years old have diabetes
- **PREVALENCE AMONG SENIORS:** **7 million** Americans 65 years old or older have diabetes, 20.1% of this age group
- **PREVALENCE BY GENDER:** 7.8 million men have diabetes, **8.3% of the male population**. 9.1 million women have diabetes, **8.9% of females**
- **NEW CASES DIAGNOSED ANNUALLY:** **1 million people** 20 years old or older
- **INSULIN USE:** Adults with diagnosed diabetes, **11% take insulin and oral medications, 22% take insulin only**, 49% take oral medications only, and 17% do not take insulin or oral medications
- **DEATHS AMONG PEOPLE WITH DIABETES:** Diabetes was the **fifth leading cause of death** in the U.S. in 1999. The risk for death among people with diabetes is about 2 times that of people without the disease. In 1999, about 450,000 deaths occurred in people 25 years old or older with diabetes
- **COMPLICATIONS OF DIABETES:** Heart disease, stroke, high blood pressure, blindness, kidney disease, nervous system diseases, amputations, biochemical imbalances, and susceptibility to many other illnesses, etc.
- **COST OF DIABETES IN U.S.:** Direct medical costs — \$44 billion; indirect costs — \$54 billion. **Total cost — \$98 billion**

Sources: Centers for Disease Control and Prevention, Atlanta, and The American Diabetes Association, Alexandria, Va.

Exubera is delivered before meals through a dry-powder, pulmonary inhalation system. The insulin is designed to be absorbed into the bloodstream quickly to reduce meal-related spikes in glucose levels. Clinical trials to date have shown that in type 1 and type 2 patients, Exubera is equivalent to insulin injections.

“Type 2 patients demonstrated improved glycemic control with Exubera when used alone or in combination with oral agents,” says Melissa Feltmann, a spokesperson for Aventis. “These type 2 patients reported greater overall treatment satisfaction and acceptance of Exubera compared with oral agents. In type 1 patients, data indicated that reducing the number of injections through an alternative delivery system, such as inhalation, greatly enhanced patient satisfaction, quality of life, and acceptance of intensive insulin therapy without compromising blood-sugar control.”

Phase III clinical trials for Exubera have been completed, however, the companies are conducting additional long-term studies because of small non-progressive differences in pulmonary function tests without clinical manifestation between a limited group of Exubera and control patients. The additional trials include rigorous testing and assessment of all pulmonary function measures.

Novo Nordisk and Aradigm Corp. also are developing an inhalable insulin product — NN1998, the AERx insulin Diabetes Management System. Phase III clinical trials for the system, which delivers mealtime insulin, began in September.

The AERx electronic platform guides users to inhale correctly, ensuring the drug is delivered at the right time in the breath. Based on a proprietary liquid formulation of insulin and the AERx iDMS Strip, the system converts the liquid into fine aerosolized particles to be delivered locally to the deep lung and thereby to the systemic circulation.

Executives at Novo Nordisk believe the key advantages of their pulmonary insulin product are a patented breath-check function, ensuring high predictability from dose to dose; one-unit increments; and a liquid formulation, as opposed to powder that may cause coughing in some patients.

Other pulmonary insulin products in development include Aerodose, an insulin inhaler in Phase II development by Aerogen Inc.; an inhaled formulation of insulin in early-phase studies by Alkermes and Eli Lilly & Co., based on Alkermes' AIR pulmonary drug-delivery technology; and the Bio-Air inhaled insulin product in preclinical studies by BioSante Pharmaceuticals Inc., which also is investigating the oral delivery of insulin.

## ORAL ADVANTAGE

The launch of an oral insulin delivery system is not expected in the U.S. until 2007. Industry watchers believe oral delivery is likely to be the most successful method of insulin delivery, despite inhaled insulin's advantage as far as market launch date.

“There is no doubt that oral insulin will be the most successful insulin delivery method,” Mr. Baid says. “This will lead to the transformation and the expansion of the market. The easiest or least complicated method of taking any medication is orally. People don't hesitate to take a pill if it is safe and doesn't cause any side effects.”

Although oral insulin products currently in development only will address mealtime insulin needs, analysts expect that it will be very well received.

“No one will take an injection if they can have oral insulin,” says Max Herrmann, head of healthcare at ING Financial Markets. “We believe an oral insulin will generate more than a billion dollars.”

Until recently, insulin was unable to be administered orally because it is destroyed by the acid in the stomach and the action of enzymes in the intestine. Several companies have been working on ways to deliver insulin orally, including modifying the insulin and developing a delivery agent.

In a healthy person, insulin secreted by the pancreas enters the portal vein and first targets the liver. The liver plays a critical role in the management of blood glucose, and other functions, including the metabolism of fatty acids and amino acids. An orally delivered capsule or tablet is expected to have advantages over injectable delivery options because it is delivered directly to the portal vein and then to the liver, which is consistent with the body's normal physiology and prevents residual insulin from lingering in the body. Excess insulin in the body is commonly associated with toxicity and other factors such as hypoglycemia.

“Oral insulin eliminates many of the downsides of current insulin therapy,” Dr. Goldberg says. Leaders in the development of oral insulin products include co-developers Nobex Corp. and



GlaxoSmithKline, and Emisphere Technologies Inc. — both with products in Phase I/II development for mealtime insulin.

In May 2002, Nobex Corp. and GlaxoSmithKline entered into an alliance for the development

## History of Diabetes

**DIABETES HAS BEEN RECOGNIZED AS A MEDICAL CONDITION FOR AT LEAST 3,500 YEARS, BUT THE CAUSE OF THE DISEASE WAS UNKNOWN UNTIL THE EARLY 1900S.** In ancient times, physicians diagnosed diabetes by the sweet taste in the urine that was caused by the presence of large amounts of sugar.

Before the discovery of insulin, people with type 1 diabetes died from a lack of insulin. In the fall of 1920, at the University of Toronto, Dr. Frederick Banting and Dr. Charles Best were able to make a pancreatic extract which had anti-diabetic characteristics. They were successful in testing their extract on diabetic dogs. With the help of Canadian researchers J.J.R. MacLeod and J.B. Collip, the scientists were able to purify insulin for use on diabetic patients. The first tests were conducted on a teenager with diabetes in early 1922 and were a success.

"Insulin represents the first biotech product," says Michael Goldberg, M.D., Chairman and CEO of Emisphere Technologies. "Insulin was the first protein to be administered, as well as the first recombinant protein to be commercialized. It is a great model compound when discussing the need for improved delivery of biotech and macro molecules."

Insulin is a hormone, and therefore, a protein. Insulin is secreted by groups of cells within the pancreas called islet cells. The pancreas has functions in addition to insulin production, including the production of digestive enzymes and other hormones. Carbohydrates are absorbed from the intestines into the bloodstream after a meal. Insulin is then secreted by the pan-

creas in response to this detected increase in blood sugar. Most cells of the body have insulin receptors, which bind the insulin that is in the circulation. When a cell has insulin attached to its surface, the cell activates other receptors designed to absorb glucose from the blood stream into the inside of the cell.

Without insulin, a person can eat a lot of food and still be in a state of starvation since cells cannot access the calories contained in the glucose without the action of insulin.

In 1959, scientists identified two types of diabetes: patients with type 1 diabetes were typically young and lacked insulin, those with type 2 diabetes were usually older and had problems producing or using the insulin their bodies produced.

People of all ages can develop type 1 diabetes, but adolescents and young people are at the highest risk. Patients with type 1 diabetes require insulin injections throughout the day.

Type 2 diabetics are those who develop insulin resistance instead of having a true deficiency of insulin. Type 2 diabetes is the result of a combination of genetic and external factors, including reduced physical activity and an increased consumption of calories, especially fat. Type 2 diabetes traditionally has affected adults older than 40 years, but also is beginning to appear in children.

In type 2 diabetics, the levels of insulin in the blood are similar or even a little higher than in normal, non-diabetic individuals. The cells of type 2 diabetics respond sluggishly to the insulin they make and their cells cannot absorb the sugar molecules, leading to blood sugar levels that run higher than normal.



**THERE ARE A LOT OF COMPANIES THAT ARE WORKING ON NON-INJECTABLE INSULIN AND THERE HAVE BEEN A LOT OF COMPANIES THAT HAVE FAILED. THIS IS A HIGH-RISK PROJECT, BUT THE REWARDS, IF SUCCESSFUL, WILL BE ENORMOUS.**

**MAX HERRMANN**



WE BELIEVE THAT FOR INSULIN USERS WHO CUT BACK ON THEIR INJECTIONS DUE TO NEEDLE PHOBIA, THE CONVENIENCE PROVIDED BY AERX MAY HELP PATIENTS BETTER COMPLY WITH THEIR TREATMENT REGIMENS.

**DR. MADS  
KROSGAARD  
THOMSEN**

and commercialization of orally administered insulin products for the treatment of diabetes. The companies have developed a modified insulin based on Nobex's patented polymer technology. The objectives of the approach are to provide multiple, new physical and chemical characteristics to drug molecules to enable oral delivery. The company has attached low-molecular-weight polymers at specific sites on the molecule to create a conjugated drug-polymer molecule. This new insulin molecule is not degraded as readily by enzymes in the body and is absorbed more efficiently across the gastrointestinal wall, compared with the drug in its native form.

"We are the first company to embrace the notion that one can change the structure of the insulin molecule to achieve oral drug delivery by providing the insulin molecule with new physiochemical and biological properties that it didn't have before that are related to enabling it to be delivered by the oral route," says Christopher Price, Ph.D., president and CEO of Nobex Corp.

The industry's previous attempts to bring an oral insulin product to market have met with failure, which Dr. Price attributes to the approach taken.

"We think the approach we've taken, of optimizing the insulin molecule and then putting it into a formulation for oral delivery, is the difference that will make us successful," Dr. Price says.

Emisphere Technologies' oral insulin product does not use a modified insulin molecule, but uses commercially existing, readily available insulin and packages it in a formulation that can withstand the enzymes in the stomach and be absorbed safely with commercially relevant efficiency.

"We believe that we are the only company in the world that can deliver, safely and effectively, physiologic recombinant human insulin unchanged from what everyone who produces insulin produces naturally, without any modification at all to the insulin," Dr. Goldberg says.

Emisphere has developed its product through Phase II trials and is in the process of negotiating a partnership agreement for additional trials and marketing.

While inhalable and oral delivery options are the most advanced non-injectable insulin products, a transdermal insulin delivery system is also being developed. Altea Development Corp. is working on a patch-based system that enables convenient, controlled delivery of a wide range of drugs including proteins, such as insulin.

Unlike many of the other systems in development, Altea's patch will provide a 24-hour, steady delivery of unmodified insulin that would replace the one or two daily injections of long-acting insulin used by individuals with diabetes.

"For many patients with type 2 diabetes, the only insulin therapy they will ever go on would be a once-daily, after dinnertime, injection of a long-acting insulin with the intent to reduce hyperglycemia," Mr. Eppstein says. "The patch will completely eliminate the need for long-acting, basal insulin injections, which for many patients with type 2 diabetes, is frequently the only insulin injection therapy used, typically in combination with oral hypoglycemic drugs. For those patients with type 1 diabetes, mealtime bolus deliveries will still be needed to maintain tight control over glucose levels after meals."

Another insulin delivery method in development is an oral spray. Oralin is Generex Biotechnology Corp.'s proprietary, engineered insulin formulation, which is delivered via a RapidMist device into the mouth and absorbed into the bloodstream through the buccal mucosa. Since 1995, Generex has been conducting studies on buccally absorbed insulin formulations. The company currently is conducting safety and efficacy trials of Oralin in humans.

## A SLOW START

For the non-injectable insulin products that receive Food and Drug Administration approval, the potential patient population is large. Currently an estimated 17 million Americans, or 6.2% of the population, have diabetes, although only about 11.1 million are diagnosed. Of that number, about 850,000 have type 1 diabetes and 10.4 million have been diagnosed with type 2 diabetes. Frost & Sullivan estimates the diabetic population in the U.S. will reach 18.9 million in 2004 and 19.5 million in 2005.

The market for insulin therapies is expanding rapidly, with total sales growing 65% from 1999 to 2001, according to data from IMS Health. Total U.S. insulin sales for 2001 totaled \$1.59 billion, IMS reports. Eli Lilly & Co. led the market for insulin products, holding a 61% share. Eli Lilly sells and markets the leading insulin product, Humulin N, which had 2001 sales of \$347.9 million.

Novo Nordisk is the second leading insulin marketer in the U.S., holding a 27% share of the

market. The company has a much stronger presence in Europe, where it is the leading insulin marketer.

If the new treatments allow physicians to start moving type 2 diabetics to insulin treatment earlier in their disease state, the new non-injectable products could take some market share from oral hypoglycemic medications.

The market for oral hypoglycemic medicines was valued at \$5.55 billion in 2001, and includes blockbuster products such as Bristol-Myers Squibb's Glucophage and GlaxoSmith-Kline's Avandia. ♦

PharmaVoice welcomes comments about this article. E-mail us at [feedback@pharmalinx.com](mailto:feedback@pharmalinx.com).

## Experts on this topic

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**JONATHAN EPPSTEIN.** President of research and chief technical officer, Altea Development Corp., Tucker, Ga.; Altea is a private company whose goal is to develop breakthrough products for biotechnology drugs as well as pain medicines that serve the unmet medical and market needs to provide patient-friendly, noninvasive patch products for proteins and vaccines, and a rapid onset patch for pain medications

**MELISSA FELTMANN.** Spokesperson, Aventis Pharmaceuticals Inc., Bridgewater, N.J.; Aventis is a world leader in the discovery, development, and marketing of innovative pharmaceutical products

**MICHAEL M. GOLDBERG, M.D.** Chairman and CEO, Emisphere Technologies Inc., Tarrytown, N.Y.; Emisphere is a biopharmaceutical company pioneering the oral delivery of otherwise injectable or inhaled drugs

**MAX HERRMANN.** Head of pharmaceutical research, ING Financial Markets, London; ING Financial Markets is a unit of ING Group, a global financial institution offering banking, insurance, and asset management to more than 50 million private, corporate, and institutional clients in 65 countries

**FRANCINE RATNER KAUFMAN, M.D.** Professor of pediatrics, Childrens Hospital

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**MADS KROGSGAARD THOMSEN, D.V.M., PH.D., D.SC.** Chief science officer and executive VP, Novo Nordisk Pharmaceuticals Inc., Princeton, N.J.; Novo Nordisk, the U.S. affiliate of Novo Nordisk AS, Copenhagen, Denmark, combines drug discovery with state-of-the-art technology to turn science into solutions for people with diabetes, people with hemophilia, and children with growth hormone deficiency



ANY TYPE OF NEW INNOVATION REINVIGORATES PEOPLE TO STICK TO A REGIMEN, SO NON-INJECTABLE INSULIN WILL HAVE SOME ADVANTAGES, BUT IT WILL CERTAINLY NOT BE THE ULTIMATE ANSWER SINCE INSULIN, GIVEN BY ANY MEANS, IS NOT THE CURE FOR DIABETES.

**DR. FRANCINE RATNER KAUFMAN**