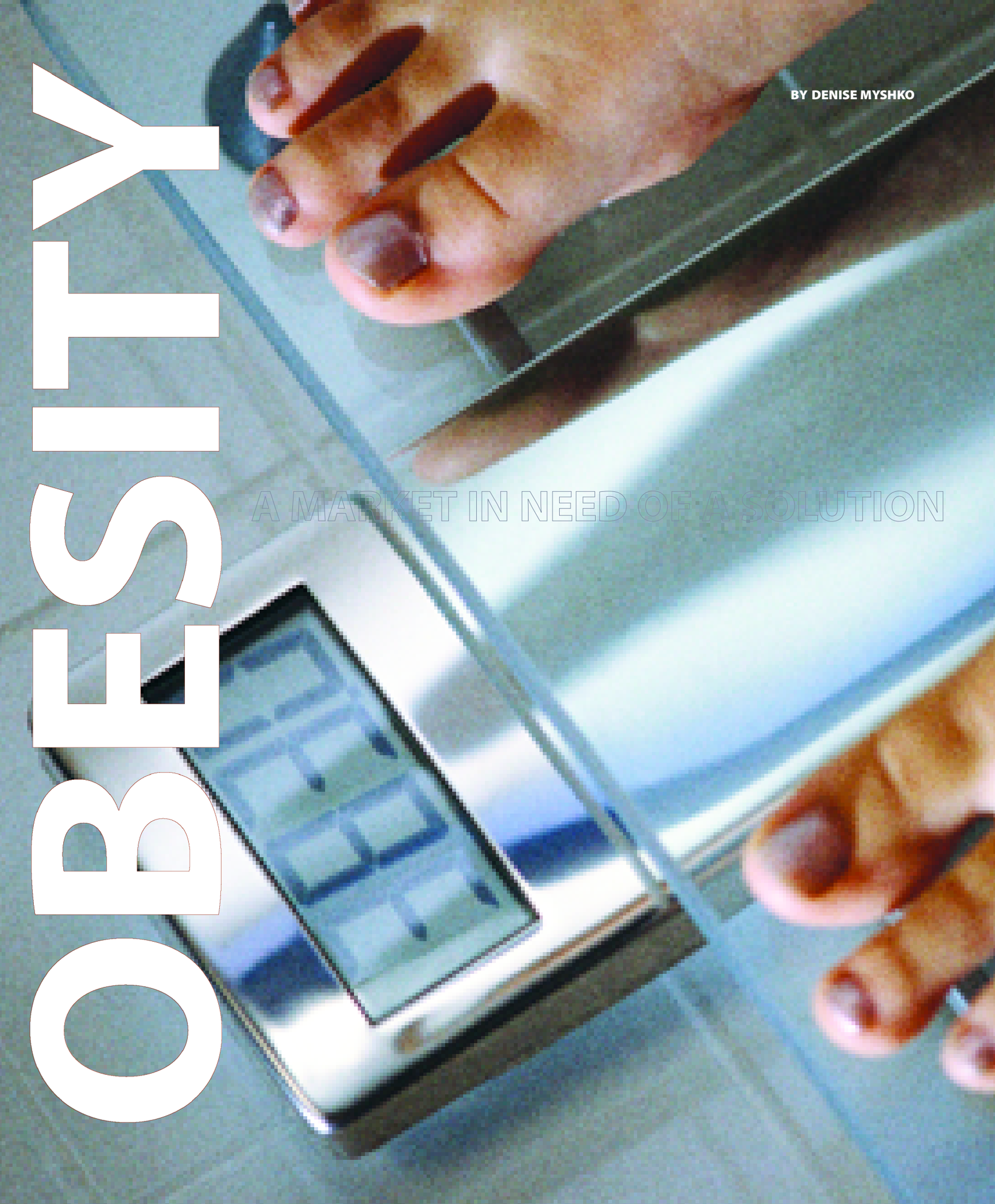
OBESITY

A MARKET IN NEED OF A SOLUTION

BY DENISE MYSHKO



WITH A POTENTIALLY OPEN MARKET FOR DRUGS TO TREAT OBESITY AND RELATED DISEASES, pharmaceutical companies not only have to provide a pharmacological solution but also address the life-style issues associated with the disease and develop safe products that are effective and have few side effects.

Take a growing patient population that is searching for a quick therapeutic fix. Add a dash of marketed drugs that have only moderate success profiles. Temper this with some skepticism amid highly publicized product withdrawals. Then stir in a regulatory agency that is considering changing its development guidelines. This becomes a recipe for a market with unmet needs.

Epidemiological studies have shown that the prevalence for obesity has increased at an alarming rate in the United States and the majority of European countries in the last 10 years. The prevalence of obesity in adults is 10% to 25% in most countries of Western Europe and 20% to 25% in some countries in the Americas. Today, an estimated 300 million people around the world are obese, and prospective studies predict that this number will continue to climb. In addition to the epidemic of obesity in the adult population, the prevalence of obesity in children is dramatically increasing. In 1999, 13% of children 6 years to 11 years old and 14% of adolescents between 12 and 19 years of age in the United States were overweight. This prevalence has nearly tripled for adolescents in the past two decades. Overweight adolescents have a 70% chance of becoming overweight or obese adults. This increases to 80% if one or both parents are overweight or obese.

Obesity is characterized by an increase in adipose tissue mass, which is difficult to quantify. In clinical practice, body fat mass is estimated by the body mass index (BMI), or waist circumference. A BMI of between 25.0 and 29.9 is considered overweight, and a BMI greater than or equal to 30.0 among adults 20 years old and older is considered obese.

Currently, 64.5% of U.S. adults, age 20 years and older, are overweight and 30.5% are obese. Severe obesity prevalence was recorded at 4.7% in the 1999 to 2000 period, up from 2.9% between 1988 and 1994, according to the Centers for Disease Control and Prevention (CDC).

Each year, obesity results in at least 300,000 deaths in the United States, and healthcare costs of American adults with obesity amount to about $100 billion, according to statistics quoted by the American Obesity Association.

DOCTORS SAY DRUGS SHOULD BE USED TO PREVENT OBESITY IN THOSE WHO ARE OVERWEIGHT AND WHO ARE AT RISK FOR OBESITY, IN COMBINATION WITH LIFE-STYLE CHANGES, SUCH AS DIET AND EXERCISE.

Debate is swirling around the actual number of obesity-related deaths. In March 2004, the U.S. Centers for Disease Control and Prevention surmised in a report published in the *Journal of the American Medical Association* that in 2000 there were 400,000 deaths in the United States (17% of all deaths) related to poor diet and physical inactivity. Only tobacco use caused more deaths, 435,000. But, following a report in the *Wall Street Journal*, the CDC has since stated that its estimate may be wrong and that it will likely submit a new, lower figure to the *Journal of the American Medical Association*.

Nevertheless, experts believe there is a strong correlation between obesity and other serious conditions such as high blood pressure, diabetes (type 2), heart disease, stroke, gallbladder disease, and cancers of the breast, prostate, and colon.

"There has been a 10-fold increase in disability claims based solely on obesity over the last six or seven years," says Robert Anfield, M.D., medical director and VP of UnumProvident Corp. "And the number of disability claimants with diabetes and hypertension has doubled in the last three years. These data track pretty well with what the CDC is reporting, which shows that type 2 diabetes has increased by about 61% over the last decade. Obesity has increased about 74% since 1991."

The principal causes of the striking rise in obesity are attributed to a combination of genetic, social, and behavioral factors and a profound change in modern life-style. Individuals may become obese if exposed to an environment where food is easily available and a sedentary life-style is promoted. Genetic predisposition might accentuate this tendency.

Analysts predict that the worldwide mar-

DR. ROBERT ANFIELD

There has been a **10-FOLD INCREASE** in disabilityclaims based solely on obesity over the last six or seven years.

ERIC FINKELSTEIN

If companies could come up with cost-effective interventions that make people healthier and save money, **THAT WOULD BE A GOOD THING NOT JUST FOR THE GOVERNMENT BUT ALSO FOR INSURERS AND EMPLOYERS.**

DR. REBECCA TAUB

I think physicians have had some reluctance to use medicines for the treatment of their obese patients. But that attitude is changing. **THERE IS AN UNDERSTANDING THAT THIS IS A TRUE DISEASE THAT CAN LEAD TO MORE SERIOUS CONDITIONS.**

ket for obesity drugs could reach $2.3 billion in 2013, up from $500 million in 2003, according to Decision Resources Inc. This reflects an annual growth rate of 17% during the 10-year study period. This will be primarily driven by the sales strength of Sanofi-Aventis' Acomplia (rimonabant). Set to launch in 2006, Acomplia is poised to become the first antiobesity agent to achieve blockbuster status.

The U.S. market for antiobesity drugs is projected at $1.7 billion in 2013, says Donny Wong, Ph.D., an analyst at Decision Resources. In 2003, the market was estimated to have been $315.5 million (See chart on page 53 for more details).

Sales of antiobesity agents in the major pharmaceutical markets (United States, France, Germany, Italy, Spain, United Kingdom, and Japan) have declined over the past two years because of safety concerns and modest efficacies of currently marketed drugs, as well as the lack of reimbursement for these agents by third-party payers, according to Decision Resources.

A study by researchers at RTI International and the CDC found U.S. obesity-attributable medical expenditures reached $75 billion in 2003 and that taxpayers finance about half of these costs through Medicare and Medicaid.

"We used nationally representative data that tracked the medical costs for one year of a group of obese people and a group of normal weight people," says Eric A. Finkelstein, associate director of the center for health promotion economics at RTI International.

The hypothesis, he says, was that if these two groups of people were the same in all respects except for obesity, then the difference in healthcare costs must be due to obesity.

"We published a second paper in January 2004 where, in essence, we reproduced those numbers and came up with state-to-state numbers," he says. "RTI found that total state-level expenditure estimates in 2003 range from $87 million in Wyoming to $7.7 billion in California. Obesity-attributable Medicaid expenditure estimates range from $23 million in Wyoming to $3.5 billion in New York. Medicare expenditures range from $15 million in Wyoming to $1.7 billion in California."

The total direct and indirect costs associated with obesity, including medical costs and lost productivity, were estimated at $117 billion nationally for 2000, according to the 2001 Surgeon General's Call to Action to Prevent and Decrease Overweight and Obesity.

The market for obesity drugs is going to be huge, says Adam Noah, research analyst, healthcare, at Granite Financial Group.

"There is going to be a market for a prescription drug that treats obesity because there are people who will always want to take a shortcut," he says. "The bottom line is that there is no magic bullet. In the end, people have to exercise and eat less, but there is clearly a subsegment of patients who need pharmaceutical help."

From an industry perspective, this is a large market with lots of opportunities, Mr. Noah says.

"This is not a situation where the winner takes all," he says. "Different drugs with different efficacies for different people and different side-effect profiles can do well. But the bar is high. Side-effect profiles have to be good. Companies will have to enroll a huge number of people in long-term studies. And just the slightest hint of anything negative will cause companies to back off."

According to Dr. Wong, one of the key drivers of the market will be Acomplia.

Acomplia is the first in a new class of drugs that targets the endocannabinoid system, which works in the "hunger center" of the brain and in other areas of the body. The product is a selective cannabinoid type 1 (CB 1) blocker being developed for the management of cardiovascular risk factors, including obesity, metabolic syndrome, dyslipidemia, type 2 diabetes, and tobacco dependence.

"Acomplia will be a big piece of the market," he says. "Keep in mind that our estimates are somewhat conservative. Some analysts predict a market of $5 billion or $6

DR. JONATHAN HAUPTMAN

Drugs should not be used to replace diet and exercise; they should be used as an addition to help people. **OBESITY IS A RELAPSING CHRONIC DISEASE. IT CAN BE TREATED BUT IT CAN'T BE CURED.**

billion, which includes worldwide sales for obesity as well as an indication for smoking cessation for Acomplia. We haven't included those estimates in our projection."

Sanofi-Aventis presented the results of its RIO-North America trial at the recent American Heart Association (AHA) Scientific Sessions meeting. The 3,040-patient Phase III study was carried out over two years with overweight or obese patients randomized to Acomplia or placebo for one year and then re-randomized for another year.

Datamonitor analysts say proof of safety and tolerability over an unlimited treatment period will be a key factor in the successful uptake of the drug, as it has already been shown that patients who were switched from treatment to placebo tended to regain any weight lost.

Additionally, Datamonitor analysts say despite data showing considerable promise for the efficacy of the drug, there was a noticeable rate of withdrawal because of depression during the trial. Given the current climate of increased regulatory scrutiny on new drugs and their safety profile after the recent Vioxx and Paxil controversies, any potential risk factors in the drug's use are likely to be investigated even more thoroughly, they say.

"The withdrawal of Vioxx from the market has changed everything," Dr. Wong says. "There also are lingering effects from fen-phen; doctors are concerned about possible side effects from new drugs."

The Decision Resources study also finds that lack of reimbursement for weight-loss therapies results in out-of-pocket expenses of about $3 per day for the two leading antiobesity agents on the market: orlistat, which is the active ingredient in Roche's Xenical, and sibutramine, the active ingredient in Abbott's Meridia and AstraZeneca's Reductil.

"The high cost of these therapies is the No. 1 reason for noncompliance and discontinuation of drug therapy," Dr. Wong says. "According to physicians who we interviewed, many patients cannot afford to refill their prescriptions. Therefore, a significant commercial opportunity exists for agents that can offer safety and efficacy profiles similar to those of orlistat and sibutramine, but at a reduced cost."

Specialists and primary-care physicians interviewed by Decision Resources say there is a lack of confidence that currently available drugs offer sufficient efficacy to merit the effort to treat obese patients. As a result, many physicians prescribe only diet and exercise for their patients and are reluctant to use pharmacotherapy.

Dr. Wong says there are more than 100 antiobesity agents in the pipeline, although just a handful are in late-stage development.

"It's only been in the last decade that researchers have come to understand the mechanisms behind obesity, and it is a very complicated process," he says. "Safety and efficacy will be significant issues for any product in development."

Additionally, patient expectations around obesity are very high, says Rebecca A. Taub, M.D., VP of research, metabolic diseases, at Roche.

"Marketing for weight-loss products often focuses on the 30 pounds in 30 days concept," she says. "We don't believe that this is realistic or safe for that matter. A combination of diet or nutrition and exercise coupled with weight-loss medicines such as Xenical can have a good effect on people's weight. That said, the Xenical trials showed that there are a percentage of people who lose about 10% of their body weight and that isn't always sufficient for the morbidly obese individual."

Roche markets Xenical, which works locally in the gastrointestinal tract to reduce dietary

Obesity Facts

- **OBESITY IS A COMPLEX, MULTIFACTORIAL CHRONIC DISEASE** involving environmental (social and cultural), genetic, physiologic, metabolic, behavioral, and psychological components. It is the second leading cause of preventable death in the United States.
- **ABOUT 127 MILLION ADULTS IN THE UNITED STATES ARE OVERWEIGHT**, 60 million are obese, and 9 million are severely obese.
- **THE NUMBER OF ADULTS WHO ARE OVERWEIGHT OR OBESE HAS CONTINUED TO INCREASE.** Currently, 64.5% of U.S. adults, age 20 years and older, are overweight and 30.5% are obese. Severe obesity prevalence is now 4.7%, up from 2.9% reported in the 1988 - 1994 National Health and Nutrition Examination Survey (NHANES) by the Centers for Disease Control and Prevention (CDC).
- **OBESITY IS ASSOCIATED WITH MORE THAN 30 MEDICAL CONDITIONS**, and scientific evidence has established a strong relationship with at least 15 of those conditions.
- **OBESITY INCREASES CARDIOVASCULAR DISEASE RISK DUE TO ITS EFFECT ON BLOOD LIPID LEVELS**. Obesity is a major risk factor for heart attack and is now recognized as such by the American Heart Association.
- **OBESITY IS ASSOCIATED WITH THE DEVELOPMENT OF OSTEOARTHRITIS** of the hand, hip, back, and especially the knee.
- **AS MANY AS 90% OF INDIVIDUALS WITH TYPE 2 DIABETES ARE REPORTED TO BE OVERWEIGHT OR OBESE.** Obesity complicates the management of type 2 diabetes by increasing insulin resistance and glucose intolerance, which makes drug treatment for type 2 diabetes less effective.
- **EARLIER ONSET OF OBESITY-RELATED DISEASES, SUCH AS TYPE 2 DIABETES**, are being reported in children and adolescents with obesity.
- **ABOUT 30.3% OF CHILDREN (AGES 6 TO 11) ARE OVERWEIGHT AND 15.3% ARE OBESE**. For adolescents (ages 12 to 19), 30.4% are overweight and 15.5% are obese.

Source: American Obesity Association, Washington, D.C. For more information, visit obesity.org.

DR. DOMINIC BEHAN

There are opinions that the FDA may at some point be willing to accept one-year efficacy data with a larger patient population, **BUT THIS ISSUE IS IN FLUX RIGHT NOW.**

DR. CAROL WALDMAN

THIS IS A MARKET IN SEARCH OF A SOLUTION. Physicians are very skeptical about the safety and effectiveness of obesity drugs, and they are concerned about the lack of patient compliance.

fat absorption by around 30% and effectively promotes weight loss. In October 2004, the FDA approved labeling that weight loss with Xenical delayed the onset of type 2 diabetes in obese patients with impaired glucose tolerance (IGT or prediabetes).

There is a large, unmet need for efficacious and safe obesity drugs, says Dominic P. Behan, Ph.D., cofounder, director, senior VP, and chief scientific officer of Arena Pharmaceuticals Inc.

Arena has a G protein-coupled receptor (GPCR) to treat obesity that is about to enter Phase II trials. The company has identified novel GPCRs that it believes regulate energy homeostasis and has drug-discovery efforts under way to identify novel drug candidates targeting GPCRs in the central nervous system and peripheral tissues that may act to reduce fat mass in human patients.

"In animal studies, we've seen selective loss of fat mass in obese animals and a decrease in the feeding response; the animal data look excellent in terms of efficacy of the compound," Dr. Behan says. "Current drugs on the market have limited efficacy and result in the order of 10% weight loss."

The company is focusing both on known and orphan GPCRs expressed in the hypothalamus, which is an area of the brain known to be critical for regulating metabolism and food intake.

The mechanisms responsible for the development of obesity were not well understood until recently. Numerous studies clearly establish the relationship between adipose tissue mass and the brain circuitry involved in the regulation of energy homeostasis. Interestingly, hypothalamic centers have been found to play a critical role both in the regulation of food intake and energy expenditure. These centers are able to sense peripheral hormones involved in the maintenance of body weight, such as insulin and leptin, and adipose tissue derived peptides. Furthermore, a number of hypothalamic expressed neuropeptides are believed to play a major role in the regulation of food intake. These neuropeptides are endogenous ligands for a number of GPCRs. Modulation of the activity of GPCRs via peptide binding has been shown to alter the hypothalamic response to food intake. In addition, several factors, including newly discovered peptides released by fat cells, have been found to play a critical role in insulin sensitivity, free fatty acid release, and signaling the brain as to fat mass levels.

A DOMINO EFFECT

According to reports, more than 50 years ago research identified that an increased body weight, especially abdominal rather than gluteo-femoral body fat, was associated with an increased risk for diabetes and cardiovascular diseases. More recently, clinical studies demonstrated that obesity significantly decreases life expectancy and strongly correlates with numerous life-threatening chronic diseases such as coronary heart disease, diabetes mellitus, stroke, and certain cancers. Obesity can increase the risk of health complications ranging from non-fatal debilitating conditions such as osteoarthritis, gallbladder disease, muscular and respiratory problems, to psychological consequences ranging from lowered self-esteem and social isolation, to clinical depression. Severe obesity is associated with a 12-fold increase in mortality in 25 to 35 year olds when compared with lean individuals.

Some of these comorbidities such as type 2 diabetes and the so-called metabolic syndrome — where there is a combination of obesity, diabetes, lipid disorders, high-blood pressure, and other disorders that are caused by, or related to, obesity itself — have to be addressed, says Dr. Taub.

"There is an understanding that this is truly a disease and can lead to even more serious diseases," Dr. Taub says.

But, currently very few people reach their weight goals by using drug products alone, says Carol Waldman, Ph.D., senior VP of NOP World Health.

"For those who do meet their goal weight, within two years most end up at their old weight," she says. "There is a high rate of recidivism. Patients can't maintain the weight loss, and they become discouraged. They've tried many things and there is no magic bullet."

Dr. Waldman says a further complication is that weight loss requires the patient to change some behaviors.

"Although there is a new drug on the horizon — Acomplia — that could go a long way toward making weight loss more possible, people also must be willing to change their behavior," she says.

The medical need to find a solution to the growing obesity problem in the United States goes beyond the problems of obesity itself.

"There is a trend now to treat the patient as a whole," Dr. Waldman says. "For example, many obese patients also suffer from metabolic syndrome. Obesity leads to insulin resistance or prediabetes, which leads to hypertension and lipid problems. The patient has a conglomeration of diseases with obesity playing a key role in their development."

Physicians consider metabolic syndrome as a key issue, with two-thirds considering the condition in their diagnosis and treatment of obese patients. According to a Market Measures/Cozint study released in May 2003, doctors report that one-fifth of the patients they see each month suffer from metabolic syndrome — defined as the presence of three or more of the following conditions: hypertension, diabetes, low HDL, high triglycerides, and obesity.

The vast majority of doctors — 94% — expect the number of patients they diagnose with the syndrome to increase in the year ahead, according to the study. This indicates that there is a growing market for new agents that treat two or more of the conditions comprising metabolic syndrome. Physicians are open to accepting both single agents and two-drug combinations that address multiple aspects of the syndrome.

The most promising prospects in obesity pharmacotherapy may lie in combination treatment.

"From a scientific perspective, it seems logical to study, for instance, tonic-appetite suppressants in conjunction with short-acting, meal-related satiogenic agents and/or thermogenic compounds," says Christian Weyer, M.D., senior director of clinical research at Amylin Pharmaceuticals Inc. "Combining agents that have different targets and different, possibly additive or even synergistic, mechanisms of action, may yield improved efficacy. At the same time, it may be possible to reduce the dosage of individual agents, which in turn could limit side effects and enhance safety."

Over the next decade, obesity treatment may follow the same evolution as treatment of other metabolic diseases, such as type 2 diabetes, hypertension, or dyslipidemia, in which combination therapy has become a standard of care.

"Defining the appropriate trial design, and identifying safe agents that are suitable for add-on, combination therapy, will be critical next steps," Dr. Weyer says. "Now might be a crucial time to lay the foundation and establish the regulatory path for this kind of approach to obesity pharmacotherapy."

Amylin Pharmaceuticals is engaged in the discovery and development of peptide hormones for metabolic disease and has several candidates in its pipeline for the potential treatment of obesity, including AC137 (pramlintide acetate) and AC162352 (synthetic PYY3-36).

AC137 is pramlintide acetate, the same active compound as Symlin, Amylin's lead drug candidate for type 1 and insulin-using type 2 diabetes. Pramlintide acetate, an analog of the cell hormone amylin, has been studied extensively in people with diabetes and, besides its effect on postprandial and overall glucose control, has been demonstrated to reduce food intake in short-term studies and body weight in long-term studies. Symlin currently is under review by the FDA with an action date of March 20, 2005. According to company statements, the results of a blinded, placebo-controlled study that included 204 obese subjects, 160 without diabetes and 44 with noninsulin-treated type 2 diabetes, showed that weight loss can be seen in obese subjects with and without diabetes.

The other potential obesity drug in Amylin's pipeline is AC162352 (synthetic PYY3-36). PYY3-36 is a naturally occurring human hormone produced by the gut, which has been reported by independent academic investigators to reduce hunger and food intake in lean and obese subjects. Amylin has published positive results from its internal preclinical program on AC162352 and has initiated Phase I clinical testing in the United States following an IND submission in December 2003.

THE OBESITY MARKET 2003-2013

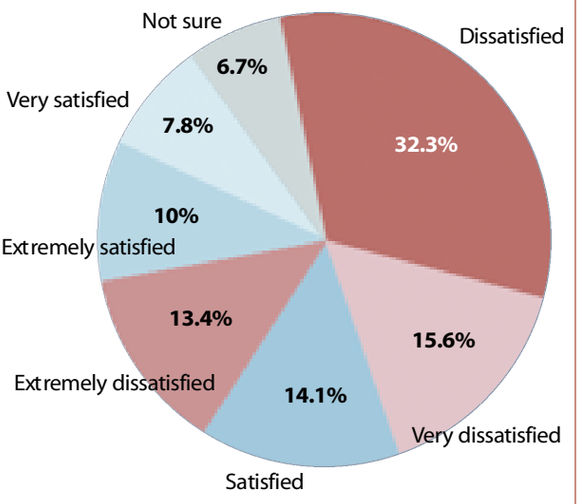
UNITED STATES	2003	2013
PREVALENT POPULATION	68,397,900	87,905,500
MARKET ($MM)	$315.5	$1,723.5
EUROPE	**2003**	**2013**
PREVALENT POPULATION	43,106,500	48,627,300
MARKET ($MM)	$177.4	$542.2
JAPAN	**2003**	**2013**
PREVALENT POPULATION	3,214,200	3,330,200
MARKET ($MM)	$5.3	$51.0

Note: Estimates for Europe cover France, Germany, Italy, Spain, and the United Kingdom.

Source: Decision Resources Inc., Waltham, Mass. For more information, visit decisionresources.com.

PATIENT SATISFACTION WITH WEIGHT LOSS DRUGS

OF THE RESPONDENTS TO A SURVEY REGARDING THEIR ATTITUDES TOWARD WEIGHT-LOSS DRUGS WHO DESCRIBED THEMSELVES AS OVERWEIGHT OR OBESE, only **29.4%** indicated that they had tried prescription drugs to lose weight. Women were more than three times as likely to have tried weight-loss drugs **(32.2%)** than men **(9.3%)**, and American respondents were more likely **(28.5%)** than British **(15.1%)** or respondents from other countries **(14.8%)**.



Source: NCERx, Carlsbad, Calif. For more information, visit ncerx.com.

LEADING DISEASE RESEARCH FUNDING

Disease	NIH Funding	U.S. Adult Prevalence
AIDS	$2.9 billion	514,000
CARDIOVASCULAR DISEASE	$2.4 billion	64 million
DIABETES	$1.1 billion	18 million
SMOKING	$566 million	46 million
OBESITY	$440 million	64 million

Source: American Obesity Association, Washington, D.C. For more information, visit obesity.org.

A REGULATORY DEBATE

During a September 2004 meeting of the Endocrine and Metabolic Advisory Committee of the Food and Drug Administration, industry and regulatory officials discussed the possibility of changing the 1996 proposed guideline requirements for the development of obesity products.

Under consideration by the committee is limiting some of the requirements to how obesity medicines are developed, Dr. Taub says.

"There are some fairly rigorous requirements

that probably don't make sense in the current atmosphere," she says. "For example, there is a requirement for a six-week lead-in to determine whether diet and exercise will result in weight loss. If weight loss occurred, the thought was that these individuals would not need medication. But it has been shown that these individuals are likely to regain that weight.

"There is a strong feeling now that diet and exercise alone will not be sufficient in a significant number of obese individuals and there will be a need for pharmaceuticals," Dr. Taub continues. "The guidelines, hopefully, will be modified to make it possible to determine the efficacy of a particular medicine."

The regulations need to change, says Jonathan B. Hauptman, M.D., director, metabolic program, at Roche.

"Since 1996, we've learned a lot about obesity," he says. "The guidance needs to keep up with what we now know about the serious health consequences of obesity."

Also under consideration is the regulatory requirement that sponsors conduct a second-year pivotal trial.

"There is no reason why a company can't demonstrate efficacy and safety in a one-year trial," Dr. Taub says. "The second-year trial involves a much smaller number of people, but it prolongs the duration of the development time line. So having that requirement is a difficult one."

"Currently, the guidance is 1,500 subjects in a trial for one year," Dr. Behan agrees. "Normally, 200 to 500 of those patients should be carried through to two years. There is some flexibility in the second year for an open-label study. But I think there is a realization that it is hard to keep these subjects engaged for two years and this may result in drop-out rates."

Dr. Hauptman says weight-loss drug trials should be considered similarly to trials for drugs that treat conditions such as hypertension or diabetes.

"We think one year for both efficacy and safety is sufficient," he says. "Right now, the FDA guidance says a year for efficacy in double-blinded trials but two years for safety. We think one year in a relatively large population should be sufficient to establish a safety profile, unless of course there are signals or early preclinical data that would make a company want to study it longer."

Additionally, he says there are several other criteria that should be reviewed.

"The first issue is who should be treated," Dr. Hauptman says. "Right now, those treated have a BMI of 30 or greater or a BMI of 27 or greater

Sound Bites from the Field

PHARMAVOICE ASKED INDUSTRY EXPERTS WHAT THE BIGGEST CHALLENGES ARE IN ADDRESSING THE OBESITY MARKET AND WHAT CAN BE DONE TO OVERCOME THESE HURDLES.

HOWARD GOLDBERG is VP and General Manager of ClinPhone Inc., Princeton, N.J., a provider of e-clinical solutions to the pharmaceutical industry. For more information, visit clinphone.com.

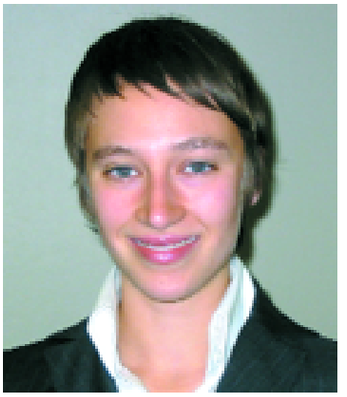
"Obesity is really a life-style issue. As Western societies, in general, lead a more sedentary life-style, the lack of exercise coupled with consumption habits lead to a general trend toward obesity. People still don't appear to be aware of the different choices they have in terms of food types, and where and what they eat. Public health initiatives should consider who people listen to and are influenced by, whether they be movie stars, celebrities, doctors, religious leaders, or activity leaders in the local community. A more personal and integrated approach needs to be taken with this messaging for it to hit home. There certainly needs to be more information made available on the benefits of exercise, along with a program of education on different types of food and their health implications. While there is a proliferation of material out there, it is impersonal, fragmented, and easy to ignore as another 'health scare' issue."

MICHAEL LIEBMAN, PH.D., is Chief Scientific Officer, Windber Research Institute, Windber, Pa., an integrated clinical, genomic, and proteomic research facility. For more information, visit wriwindber.org.

"Public-health initiatives have looked at a very small part of the obesity problem. Most of the science that comes out of NIH has been minimally interdisciplinary and non-system-oriented and therefore it focuses on a singular part of the problem rather than the problem as a whole. There is no single cause for obesity just as there are no single - gene diseases that do not exhibit additional genetic modifications. Obesity results from an interaction of home life, personal priorities, and individual health, as well as socio-economic conditions. For some people, life-style intervention may be the key and for other people, regardless of what they attempt to do at least using the current treatments, they may not be able to overcome some of the molecular issues. Just as with depression, for some people, behavior modification is enough and for others, drug therapy is required. But we shouldn't expect that there is going to be a pill to overcome their conscious actions and life-style. It's not an appropriate concept to think that there someday will be a magic pill that regardless of what life-style patients lead, it is possible to wipe out negative effects."

STEVE STRAUS is President and Chief Development Officer, Centers of Obesity Related Illness (CORI Centers), New York, which contracts with acute-care hospitals to establish bariatric surgery centers of excellence. For more information, visit weightlosssurgery.com.

"Obesity starts in childhood. It is a cultural phenomenon; 40% of our food today has transfats. As a society, we are eating less healthy food and eating a lot more of it. There is the fast-food convenience phenomena, and there is a lack of education and a lack of time to eat healthy. Education and incentives need to be put in place from a public-health standpoint. The problem is that once people get to a certain state of obesity, it is difficult to change their condition. Someone who has failed on all the popular diets, sooner or later, is going to give up. As a result, the acceptance of bariatric surgery is being embraced by more men and women. These are individuals who have failed with virtually every diet and exercise program and pharmacological approach."



ROCHELLE ELLIS

THE BIG CHALLENGE FOR PHARMACEUTICAL COMPANIES IS TO PROVE THAT THEIR DRUGS ARE SAFE; doctors and patients may be wary in light of recent events.

who have risk factors. I believe there is enough information to support dropping the BMI to 27 for everybody or alternatively to 27 without risk factors and to 25 with risk factors because people at lower levels of obesity still have consequences, especially if they have diabetes. We think the group of patients who would benefit from these drugs should be broadened."

Another important consideration, he says, is the inclusion of risk factors as a potential indication for treatment.

"We know doctors are more likely to treat patients for obesity when they also have hypertension or diabetes or hyperlipidemia," he says. "Right now, the FDA doesn't allow sponsors to say weight-loss drugs are potential treatments for these risk factors. We think that if companies conduct a study and can show results indicating that there is an improvement in diabetes or blood pressure, that should be considered as an indication, regardless of the mechanism. The FDA wants to look at the risk factors as being independent of weight loss, and we think that is wrong. We think the mechanism for improving the risk factors is not what drives the indication; it's whether the risk factors improve on treatment or not. That's very important."

One of the big challenges for companies developing obesity drugs is to prove that their products are safe, says Rochelle Ellis, an analyst with Navigant Consulting Inc.

"Meridia has been withdrawn from the market outside the United States, and patient advocacy groups are asking that it be withdrawn from U.S. market," she says.

According to published sources, Meridia has been removed from the market in Italy and is under investigation in France, Britain, and Canada.

In a July 2004 written response to the U.S. District Court for the Northern District of Ohio's ruling dismissing 113 cases against the antiobesity drug, Abbott stated that Meridia has been approved as a safe and effective treatment for obesity when combined with diet and exercise and has been extensively studied in more than 100 clinical trials involving more than 12,000 patients throughout the world. About 13 million patients in more than 70 countries have used sibutramine for the treatment of obesity; Meridia was approved in the United States in 1997.

"Drugs have their place but not for those who are severely obese," Ms. Ellis says. "We interviewed bariatric surgeons whose patients were severely obese and who came to them after the pharmaceutical treatment didn't work. The doctors I spoke with said drugs should be used to prevent obesity in those who are overweight and who are at risk for obesity, in combination with life-style changes, such as diet and exercise."✦

PharmaVoice welcomes comments about this article. E-mail us at feedback@pharmavoice.com.

Experts on this topic

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