In the pediatric setting, I believe that Madeira as well as others committed to this arena have the responsibility of educating physicians as to how a drug should be used and what role it plays in a patient's life.

Madeira Therapeutics' **PETER JOINER**

Presents a Case for the Pediatric Market

As the obesity epidemic affects more young children, the need for medicines to deal with the effects of obesity becomes more pressing. Peter Joiner started Madeira Therapeutics with the goal of developing therapies currently approved for adults for the pediatric market.

Mr. Joiner has long recognized the need for improving medicines for children by ensuring they are appropriately tested.

CAREER Highlights

Peter Joiner is CEO and President of Madeira Therapeutics. He has a 30-year history in sales, sales management, and marketing in the pharmaceutical industry. His positions have included executive-level salesforce management, strategic business planning, business analysis, and large customer account management. He has launched more than 15 major pharmaceutical products and established significant partnerships and relationships with key organizations in the healthcare industry. Before starting Madeira he was VP of managed markets at Alliant Pharmaceuticals. Before that, he spent 27 years at Sanofi-Aventis in various capacities. Mr. Joiner has a B.S. in electrical engineering and an MBA in industrial management from the University of Cincinnati.

UNCOVERING DETERRENTS

What are the major deterrents to conducting pediatric studies and entering this market?

JOINER: The challenges facing the pediatrics market fall into four categories: ethics, economics, logistics, and technical considerations. These categories were indentified in 2006 at a workshop — Addressing the Barriers to Pediatric Drug Development — held by the Institute of Medicine's Forum on Drug Discovery, Development, and Translation.

The ethical dilemma relates to physicians. Traditionally, companies have not developed pediatric labeling information, which means physicians have to prescribe an adult medication for a child and have to guess at the dosage and determine whether the formulation is right for the child, or they forgo prescribing a therapy and the child goes without a much-needed medication. There are processes for testing drugs for adult usage; children should have the same advantages. And right now most of the time they don't; when they leave the doctor's office with a prescription, 75% of the time it's for an off-label use. So, children aren't getting the same deal as adults.

In any industry, product development is driven by economics. The reality is that in evaluating children as a patient population, pharmaceutical companies take into account that children grow up, their metabolism rates change as they grow, and before long they will outgrow the drug, so it's unlikely there would ever be a blockbuster drug in this category. And large pharmaceutical companies are really interested in big blockbuster drugs. But for a smaller-scale company, there can be an economic return for servicing this market.

From a logistical standpoint, companies need to have extensive infrastructure in place to conduct pediatric drug trials, which is a barrier.

From a technical point of view, compound stability is a big issue. Certain compounds may not work in a liquid format, but for children this type of formulation might be the most appropriate. And it has to taste good; the child may take the drug the first time, but if the taste is bad, it's difficult to get him or her to take it again.

FINDING THE NEEDS

What are the most pressing needs in the pediatric market?

JOINER: Traditionally, pediatric pharmaceuticals have focused on the therapeutic areas of respiratory, including asthma; attention deficit disorder; and antibiotics. But because of the obesity epidemic, the most pressing need now is in the area of metabolic compounds — drugs such as lipid lowering statins, hypertension products, and diabetes medicines. Research shows that 30% of children are overweight and 17% have been categorized as obese. Unfortunately, as a result we're starting to see more younger people develop Type 2 diabetes, which was rare in the past.

DISCOVERING THE RISKS

What are some of the biggest risks with regard to the way children are currently treated for a variety of conditions?

JOINER: There are always risks when using a drug that hasn't been tested to be efficacious in children. For example, in the area of pain, research in the past few years has shown that younger patients who are given codeine, which is one of the choices for severe pain, aren't able to metabolize the drug appropriately because of their liver function; therefore, they don't receive the necessary relief.

When using an adult drug in a child, because of different metabolism and clearance rates, they are often not effective. In fact, sometimes the child needs more of the active pharmaceutical ingredient than an adult would because their liver clearance or metabolism rate is greater than an adult's.

Also using a drug in a child before it's been tested means that it is impossible to know what side effects may occur. Research shows that an estimated 10% of children suffer an adverse event from a drug while in the hospital setting. Dennis Quaid's newborn twins were given a blood thinner in the wrong dosage form at Cedars-Sinai Medical Center in 2007. There are many other high-profile cases such as this.

SHIFTING THE BALANCE

What is Madeira doing to address the imbalances in pediatric drug development?

JOINER: As a Kansas-based company, we work with Children's Mercy Hospitals and Clinics in Kansas City, which is a leader in this area, to develop appropriate clinical settings for testing drugs.

Children's Mercy President and CEO Rand O'Donnell has set up a group called the IPI, the Institute for Pediatric Innovation, in which five children's hospitals are working together to help commercial companies bring pediatric drugs, as well as medical devices, to the marketplace.

The FDA and NIH have a list of about 400 compounds for which they would like to have pediatric labeling information developed. Certainly Congress and the FDA have done their part, enacting legislation over the last several years, but this still has not encouraged many pharmaceutical companies to get into this marketplace. (To read more about the role companies can play to address child health issues, see PV's bonus digital text.)

In Madeira's case, we will take adult drugs that are off-patent and put them through a formulation change, following the 505(b)(2) process to make them compatible for children. These are not new chemical entities, so there are safety and efficacy data already known. ✦

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BROADENING PHARMA'S ROLE IN CHILDREN'S HEALTH

Madeira Therapeutic's CEO Peter Joiner talks to PharmaVOICE about how companies in the pediatrics space can play a role in improving children's health at all levels.

Pharmaceutical companies have played an important role educating patients about lifestyle issues, but mostly in the adult setting. Children issues are discussed much less frequently.

"I believe Madeira and other companies in this arena have the responsibility to educate physicians as to how drugs should be used in the pediatric arena," Mr. Joiner says. "For example, with statins there may be a period where a child is put on a cholesterol-reducing drug until some lifestyle modifications are made; so the emphasis needs to be on using the drug to lower LDL until changes are made in exercise and eating habits. The exception of course would be in the case of children who have a genetic defect; they would obviously use statins for the long term. Pharmaceutical companies can play a key role in promoting healthy lifestyles not just for adults but for children as well.

> I believe that in the United States, we need to take a strong look at lifestyle issues.

"I believe that in the United States, we need to take a strong look at lifestyle issues," he continues. "I read an article recently that stated that Japan is measuring older adults for the circumference of their waistline and those who exceed the recommendations face a penalty. I don't expect anything like this will happen here, but we need to be serious about our lifestyle as we go forward. Medical care is very expensive and we're not going to be able to keep up with these costs, if our citizens don't maintain a healthy lifestyle, this applies to children too."

According to Mr. Joiner, in addition to obesity issues and the accompanying conditions associated with this growing epidemic, pediatric patients are developing kidney stones an increasing rate of incidence.

"A recent study shows urologists are seeing one to two pediatric patients a week for kidney stones, when just a few years ago this was not the case," he says. "This is being attributed to the high sodium content in fast foods. That's not to say children should never eat fast foods; it's more a matter of how much they eat of any one thing."

He believes the industry can certainly play a role in changing practices.

"For example, I was involved previously with another pediatric start-up company called Alliant Pharmaceuticals in Georgia, which we sold in 2007," Mr. Joiner says. "While I was there, the company had a head lice product. We would conduct educational programs with school nurses on the issue of head lice. Many people believe head lice is associated with social economic situations, but that's not the case. Anybody can get head lice; in fact in the United States there are 6 million to 12 million cases a year."

Mr. Joiner says Madeira is not at the point of developing educational content around a marketed product yet, but he does expect the company to play a role in providing information related to pediatric dosing and issues in the future. ✦

GUIDELINES SHOW NEED FOR CHOLESTEROL-FIGHTING DRUGS FOR CHILDREN

The American Academy of Pediatrics (AAP) released new guidelines on July 7, 2008, recommending that some children as young as 8 years old be given cholesterol-fighting drugs to ward off future heart problems. It is the strongest guidance ever given by the AAP. Madeira Therapeutics, a pediatric drug-development company, currently has a statin, a cholesterol-lowering product, in the development pipeline focused on this need. The new guidelines set by the AAP are based on evidence showing that damage leading to heart disease, the nation's leading killer, begins early in life.

"Our statin product focuses on a true case of need in a population with an inherited cholesterol gene that often leads to early heart disease," says Peter Joiner, CEO and president of Madeira Therapeutics. "We are proud to be in a position to bring a much needed drug to the pediatric population; pediatric medication has been an area neglected for far too long."

Children who are at least 8 years old and have too much LDL, the "bad" cholesterol, along with other risky conditions, including obesity and high blood pressure, should be considered for cholesterol-lowering drugs. Pediatricians should routinely check the cholesterol of children with a family history of inherited cholesterol disease and also check children after age 2, but not later than age 10, for cholesterol levels. With one-third of U.S. children overweight and about 17% being obese, the new recommendations are important.

Madeira Therapeutics specializes in pediatric medicine by reformulating compounds currently approved for adults and determining an accurate pediatric dosage. Often adult drugs are prescribed by weight, but children metabolize some drugs differently than adults. Madeira focuses on reformulating off-patent adult drugs using the FDA's 505(b)(2) approval pathway. It is one of the few drug development companies with a dedicated focus on this niche market. In addition to the cholesterol-lowering drug already in the development pipeline, the company has plans to develop formulations for acute pain management and diabetes.

Source: Madeira Therapeutics. For more information, visit madeiratherapeutics.com.