# Push to spur more drugs for deadly rare diseases

April 25 2011, By LAURAN NEERGAARD , AP Medical Writer

The Hempels, from left, Cassidy, 6, her father Hugh, mother Chris and twin sister Addison gather in the lobby at the Children's Hospital and Research Center in Oakland, Calif., Friday, March 18, 2011. The Hempel twins are receiving alternative treatment for Niemann Pick Type C disease, a rare disorder where harmful amounts of cholesterol accumulates in vital organs. Every other week, 7-year-old twins Addison and Cassidy Hempel have an experimental medicine injected into their spines in hopes of battling a fatal neurologic disease. It's not a drug company study _ their mother won a government OK for the unusual exeriment. (AP Photo/Marcio Jose Sanchez)

(AP) -- Every other week, 7-year-old twins Addison and Cassidy Hempel have an experimental medicine injected into their spines in hopes of battling a rare, fatal disease.

And it's their mom who made that possible.

From her home in Reno, Nev., Chris Hempel persuaded scientists to share their research and managed to get the government to sign off on her daughters' unusual experiment. Hempel says getting help to fight a rare disease shouldn't be so hard.

But it's a huge challenge to generate drug company interest in the expensive testing of medicines for diseases so rare - like her girls' Niemann-Pick Type C - that the market is only a few hundred or few thousand people a year.

There are treatments for just 200 of the roughly 7,000 rare diseases, illnesses that affect fewer than 200,000 people, often far, far fewer. Yet add those diseases together, and more than 20 million Americans have one.

Now a movement is beginning to spur more rare-disease treatments: The National Institutes of Health this fall will open a center to speed genetic discoveries into usable therapies, doing some of the riskiest early-stage research in hopes companies then will step in.

A new International Rare Diseases Research Consortium is pushing for at least 200 more treatments by 2020, in part by pooling the work of far-flung scientists and families.

Rather than starting from scratch, the Food and Drug Administration is pointing the way for manufacturers to "repurpose" old drugs for new use against rare diseases, publishing a list of those deemed particularly promising.

And bipartisan legislation recently introduced in the Senate, called the Creating Hope Act, would offer drug makers another financial incentive - a voucher promising fast FDA evaluation of their next blockbuster drug in return for developing a therapy for a rare or neglected disease

that disproportionately affects children. It's unclear what the prospects for passage are.

"We have to give drug companies a reason to go into this market," says Nancy Goodman of Kids v Cancer, a group pushing the legislation. Her son Jacob died at age 10 from a type of brain cancer that has no good treatment.

"My kids may not be curable, but they are treatable," adds Hempel, the Nevada mom. "Who's going to take this over?"

Pharmaceutical giants are starting to show some new interest in rare diseases, traditionally a niche market for small biotech companies. The practical reason: Blockbusters are drying up, says Dr. Ed Mascioli of Pfizer Inc., the world's largest drug company.

"The industry as a whole has a pipeline problem. It's increasingly difficult to develop drugs for common diseases," says Mascioli. He heads a separate research unit that Pfizer opened last year to search for medications for certain distinctively gene-based rare diseases, such as muscular dystrophy and hereditary emphysema.

Some other companies, including Novartis AG and GlaxoSmithKline PLC, also have begun rare-disease programs.

But NIH Director Dr. Francis Collins says all the activity also reflects a larger promise. "Getting a home run with a rare disease sometimes points you in a direction that will be beneficial for common diseases," he told The Associated Press.

That's Chris Hempel's argument: Niemann-Pick Type C, or NPC, causes cholesterol and other fats to build up to toxic levels inside cells, harming various organs and especially the brain until patients lose the ability to

talk, walk and swallow. Only 500 children worldwide are known to have it. But a drug that could flush out that build-up, Hempel contends, just might point to a new route to fighting heart disease or Alzheimer's.

For NPC, Hempel hopes to repurpose cyclodextrin, a sugar-like compound that's already used in numerous products. But by itself, it wasn't deemed to have any drug effects - until scientists at the University of Texas Southwestern Medical Center made the surprise finding that cyclodextrin helped mice with NPC.

When her daughters were diagnosed in late 2007, Hempel desperately searched scientific journals for any hint of a treatment and ran across the Texas research.

What works in mice often fails in people, and it can take years of additional research before animal experiments lead to human studies.

"They don't have years," says Dr. Caroline Hastings of Children's Hospital & Research Center Oakland in California, who leads the twins' cyclodextrin treatment. "They really had nothing to lose."

Subsequent studies in cats at the University of Pennsylvania show promise, too. Hempel found a Florida supplier of cyclodextrin, and worked with Hastings to file FDA applications for "compassionate use" testing of cyclodextrin in the twins. She even persuaded Johnson & Johnson, which uses cyclodextrin as an inactive ingredient in an anti-fungal medicine, to share proprietary data about the compound's human safety and other issues to address FDA questions.

Addison and Cassidy already have serious symptoms; they'd quit talking. The cyclodextrin was first infused into their bloodstreams in 2009, but Hempel says it wasn't penetrating the brain. So late last year, FDA allowed injections into the spinal fluid, which bathes the brain. It's too

soon to know how they'll fare, but the family thinks the girls are more alert, and Hastings says tests show their hearing has improved.

Now, the NIH is planning a formal study of cyclodextrin in a number of NPC patients, to begin within about a year.

Hempel isn't alone in her quest to repurpose common drugs. Consider progeria, a disease that rapidly ages children until they die of a heart attack or stroke, usually before their teens.

Collins' lab at NIH uncovered the gene defect behind progeria, research that he says he pursued only because of meeting another mom, Dr. Leslie Gordon, founder of the Progeria Research Foundation, and her son, Sam, who has the disease. Today, clinical trials are under way using a failed cancer drug named lonafarnib that promises to block some of the progeria mutation's effect.

"We're very excited about the opportunities in progeria," says Dr. Gary Gilliland of Merck & Co., which donates the drug and is watching carefully to see if the studies make further pursuit worthwhile.

There are an estimated 150 progeria patients worldwide, but Gordon points to growing evidence that the culprit protein may play a role in the heart disease that comes with regular aging, too.

However, progress is slow. Just because initial research shows a drug looks promising doesn't guarantee broader testing. For example, a National Cancer Institute-funded team is pushing to test a certain class of drugs against a childhood cancer, Ewing's sarcoma. But none of half a dozen manufacturers has yet agreed to provide the drugs, says Dr. Peter Adamson of the Children's Hospital of Philadelphia. The reason, he says: They're not showing enough promise in more common adult cancers.