Influenza Attack! New Vaccine Strategy: Just What the Doctor Ordered—Page 7

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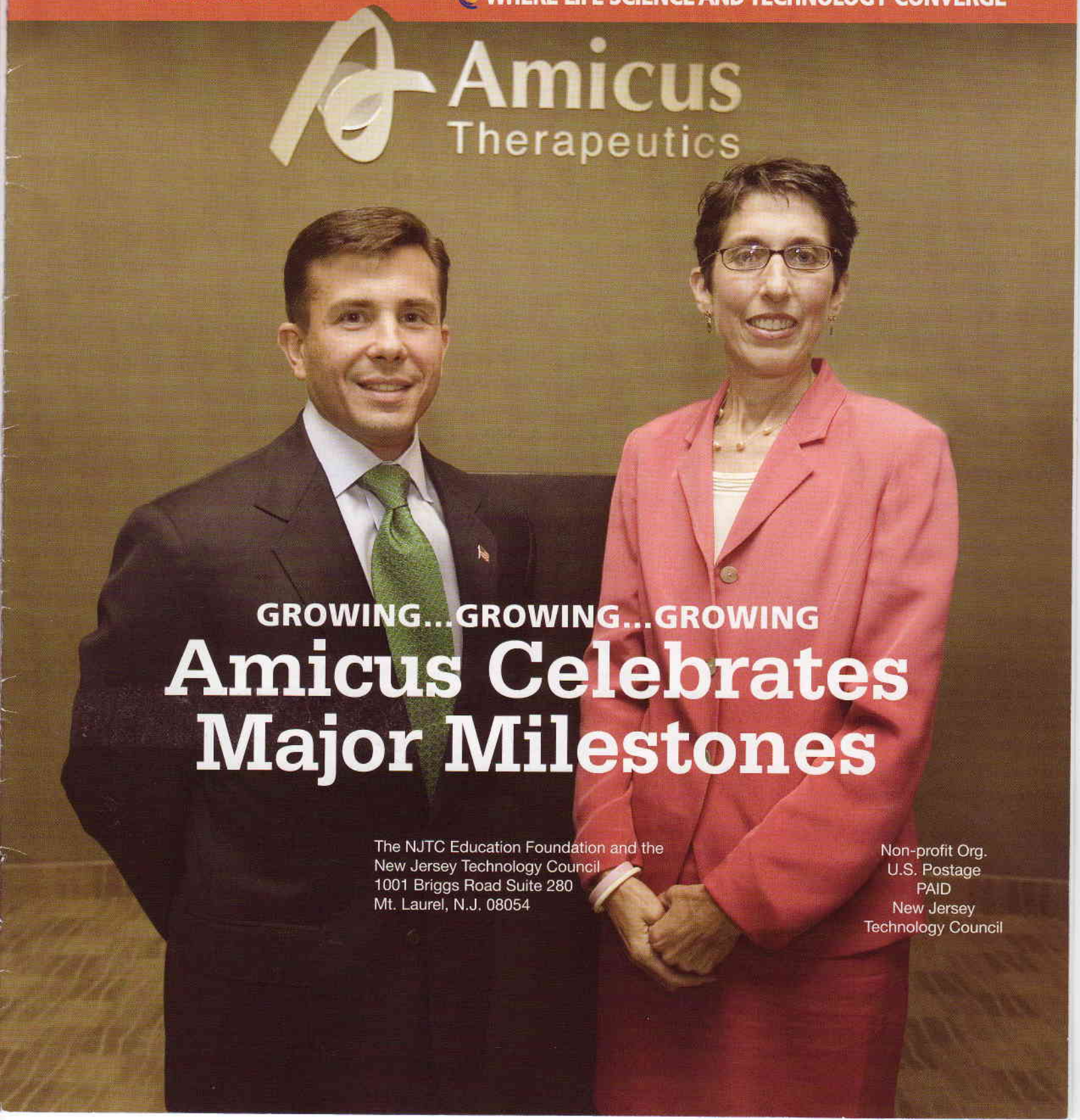

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Amicus Celebrates Major Milestones

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Amicus Celebrates Major Milestones

By Beth Fand Incollingo

Dr. Raphael Schiffmann has spent much of his career working to understand and treat rare disorders, so he knows the hardships his patients endure.

Again and again, the neurologist and researcher has heard patients describe the symptoms of Fabry disease: disabling pain in the hands and feet, severe reactions to hot weather and exercise, abdominal pain and diarrhea. He's often seen patients develop heart problems or undergo kidney transplants.

So Dr. Schiffmann was pleased when he was asked to participate in the Phase 2 clinical trial of a proposed new treatment for the genetic disease. "The approach is quite encouraging," said Dr. Schiffmann, who conducted the trial from 2005 to 2007 at the National Institutes of Health in Bethesda, Md.

Based on a new method using molecules called "pharmacological chaperones," the potential treatment for Fabry disease—and sister drugs aimed at Gaucher and Pompe diseases—have focused a spotlight on the Cranbury biopharmaceutical firm developing and planning to market them, along with possible future treatments for metabolic disorders and neurodegenerative disorders like Alzheimer's and Parkinson's diseases: Amicus Therapeutics.

> **"Most rare diseases still don't have a treatment, so we appreciate the work being done by companies studying rare diseases."**
>
> – Mary Dunkle, National Organization for Rare Disorders

Founded in 2002 as a seven-person startup venture in space subsidized by the New Jersey Economic Development Authority, Amicus celebrated its 100th hire in August 2008. During the celebration, Gov. Jon S. Corzine, Rep. Rush Holt and EDA CEO Caren Franzini described the still-growing company as a New Jersey success story.

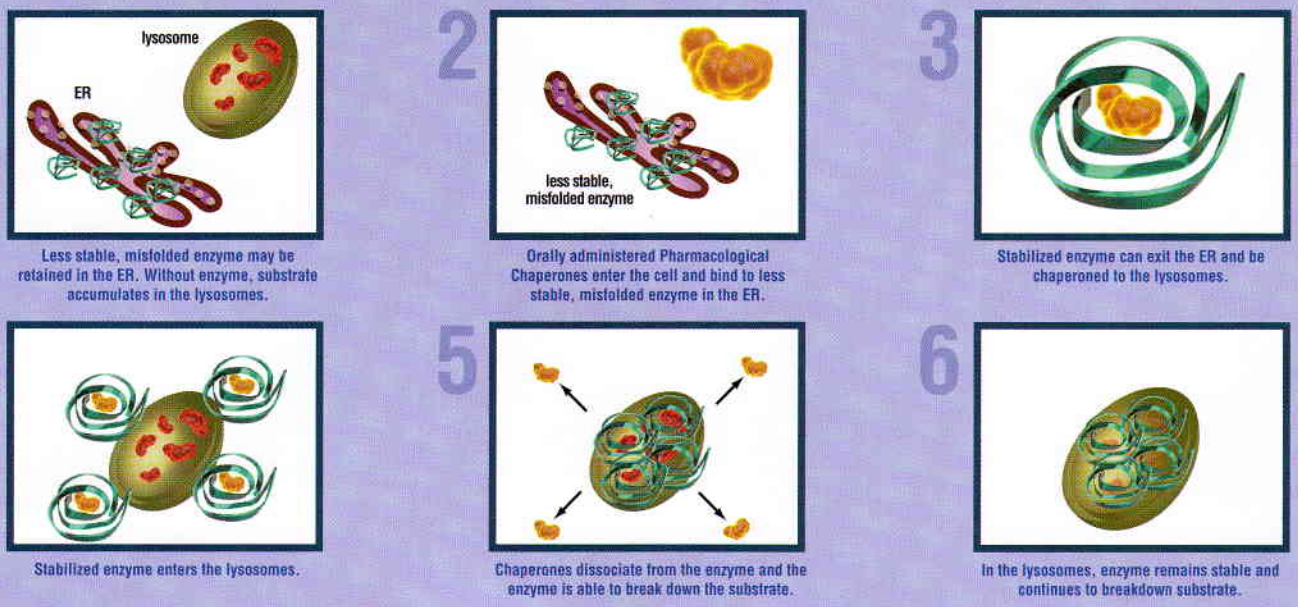
"Many companies have been researching new 'next' approaches to treating these diseases," said John Crowley, Amicus' president and CEO, "but I believe Amicus offers a dynamic approach to treating these disorders. We have a chance to shift the paradigm in how we think about treating these very rare diseases and open up a world of opportunities in how we look at a range of more common disorders."

With the company making rapid progress in its development of potential treatments and scientists, physicians and investors showing increasing interest in its work, Amicus has quickly taken its place as a player of note in the biopharmaceutical industry.

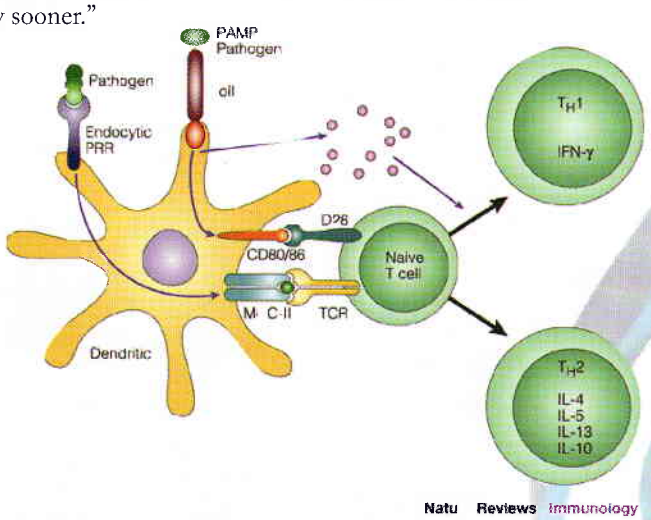
In 2007, in addition to raising additional investment capital through its initial public offering, Amicus entered into a collaboration valued at up to $440 million with Shire Human Genetic Therapies to help develop its three lead products. The same year, Amicus attracted the attention of the Michael J. Fox Foundation for Parkinson's Research, which gave the company a research grant.

Proposed Mechanisms for Pharmacological Chaperones in Lysosomal Storage Disorders

Lysosomal Storage Disorders result from genetic mutations in lysosomal enzymes that lead to reduced enzyme activity and subsequent substrate accumulation in lysosomes. Lysosomal enzymes are made in the Endoplasmic Reticulum (ER) and need to be trafficked to the lysosomes where they break down substrate. Less stable or misfolded enzymes that result from genetic mutations are often retained in the ER and not trafficked efficiently to the lysosomes. Pharmacological Chaperones are designed to bind to and stabilize enzyme in the ER, helping the enzyme get from the ER to the lysosomes where the enzyme can break down substrate.



"The pharmacological chaperone idea, and the connection between protein misfolding and human diseases, have become very hot topics," said David Lockhart, Amicus' chief scientific officer. "We and others think it's an approach that's applicable not only to a few rare diseases but potentially to a range of different human genetic diseases. Part of the reason our work is attracting attention is that lots of people have interesting ideas that always seem to be 10 years away, but we have encouraging signs of the appropriate effect in Fabry patients we have studied, so this may become reality sooner."



Pharmacological chaperones work by helping defective enzymes—made within the cells of patients with certain genetic disorders—to work better and more like the "normal" versions.

Ordinarily, enzymes—or proteins—fold into compact three-dimensional shapes and then travel from one part of a cell to another to do work that is vital to body function. But genetic problems can cause enzymes to be less stable or fold incorrectly, and to be prematurely degraded or to accumulate in the wrong places in cells, leading to disease.

Pharmacological chaperones are chemicals that can bind to defective enzymes, stabilize the enzymes and shepherd them to their intended destinations. Shortly after their work is done, the chaperones disappear, allowing the "rescued" enzymes to carry out their important jobs.

Amicus scientists believe their approach may have advantages over the current standard of care for lysosomal storage diseases like Fabry disease—enzyme replacement therapy—which works by regularly infusing a healthy version of the affected enzyme into patients' bodies.

For one thing, Lockhart says, the enzymes given in replacement therapy are too big to get to certain parts of the body. As a result, that technique doesn't work on diseases that involve the brain, neurological mechanisms or the central nervous system. Pharmacological chaperones, on the other hand, are small-molecule drugs that can travel anywhere in the body.

A final advantage to chaperones is that they're given as pills, Lockhart said—unlike infused enzyme replacement therapies, which are often administered in hospitals over the course of many hours, usually every other week for life.

(Continued on pg. 15)

(Continued from pg. 11)

Lockhart cautioned that there is a key limitation to chaperones: They're not expected to work on their own in patients whose bodies don't produce even trace amounts of a targeted enzyme.

But for other patients who suffer from these diseases, he said, the drugs could help—which is why Amicus' goal is to secure worldwide approval for all three of its lead products.

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When Amicus embarks on a Phase 3 trial of its proposed Fabry treatment—something it's planning now—the company will collect hard evidence about whether its drug will abate the disease's symptoms, and how well.

Until then, those with an interest in seeing rare diseases treated will continue to embrace Amicus' decision to develop drugs for small patient populations, said Mary Dunkle of the National Organization for Rare Disorders.

"Most rare diseases still don't have a treatment, so we appreciate the work being done by companies studying rare diseases," she said. "We understand that companies who choose to work with rare diseases could have followed the easier path of developing 'me-too' drugs for common diseases."

As Amicus' Crowley pointed out, a commitment to treating rare diseases is what drives Amicus. "There are 6,000 rare diseases and, together, they are more prevalent in America than all cancers and AIDS combined. We have to tackle them one at a time," the CEO said. "In many respects, the research is helping to usher in a new era in medicine and how we think about and treat all human diseases—and that's the really exciting part."

For more information about Amicus, visit www.amicustherapeutics.com. For more information about the NJ Economic Development Authority, visit www.njeda.com.