If Approved by the FDA, FluMist Would Become First Vaccine Delivered as a Nasal Spray:

Every fall, just before the influenza season begins, tens of millions of Americans put themselves to the needle to stave off the fevers, headaches, coughs and sore throats triggered by the highly contagious virus. This year a Gaithersburg company hopes to offer a pain-free alternative to the flu shot: a vaccine delivered with a squirt in the nose.

MedImmune Inc., the Washington region's most successful biotechnology company, is pinning its ambitions for growth on FluMist, an experimental vaccine whose development began some four decades ago. The product is being reviewed by the Food and Drug Administration, which is expected to make its decision by July. If approved, FluMist would become the first vaccine delivered as a nasal spray.

MedImmune executives and Wall Street bulls believe FluMist could win FDA approval this year, possibly in time for the 2002-2003 flu season, and eventually grow into a blockbuster product with $1 billion in annual sales. MedImmune's stock, which closed at $43.32 Friday, is trading at more than 63 times earnings as investors bet on FluMist's success.

Not everyone is so bullish. In July, FluMist ran into regulatory troubles when an FDA advisory panel recommended against its approval. Large patient trials found the vaccine to be highly effective, but panel members raised questions about its safety and wanted to see more data. Some analysts doubt FluMist will win approval this year, if ever. And even if the vaccine is approved, they are skeptical about its commercial prospects.

MedImmune has become one of the nation's most profitable biotech companies, thanks to steadily rising sales of its flagship drug Synagis, which fights respiratory illness in infants. But Wall Street, which values companies by their growth potential, wants to know what's next. The 14-year-old firm answered that question in January when it paid $1.5 billion in stock to acquire Aviron, the Mountain View, Calif., maker of FluMist.

If FluMist is successful, MedImmune could join the elite ranks of biotech companies with more than one blockbuster drug, a remarkable feat in an industry where few companies turn a profit. But its failure could trigger a stock sell-off and leave MedImmune still searching for its next growth engine. MedImmune officials declined to be interviewed for this story because FluMist is under FDA review.

Influenza is among the nation's most serious public health problems. Each flu season, which runs from November to March, 35 million to 50 million Americans get sick with the flu, according to the Centers
for Disease Control. The CDC estimates that more than 100,000 Americans are hospitalized and more than 20,000 die from the flu or its complications each year.

The CDC recommends flu shots for the most vulnerable, such as the elderly and patients with chronic illness. The current vaccine uses an inactivated, or "killed," virus to stimulate immunity. A new shot is required each year because the flu virus constantly changes.

FluMist's story started more than 40 years ago when scientists at the University of Michigan began researching new flu vaccines in the aftermath of the 1958 flu pandemic that killed nearly 70,000 Americans.

In 1967, a Syrian-born epidemiologist named Hunein "John" Maassab made a breakthrough. He developed a live, "cold-adapted" flu virus that only grew at cooler temperatures in the nasal passages, which could prevent infection in the lower respiratory tract where the disease spreads. The virus was weakened so that it could stimulate immunity without causing sickness.

"Every vaccine needs a champion to get it to market. John Maassab is FluMist's champion," said Rosemary Rochford, an assistant professor at the University of Michigan's epidemiology department. She works with Maassab, who is ill and could not be interviewed. "It's been his life mission to see that the vaccine will be available to everyone. If it's approved, it would be a realization of his life's work."

In the 1970s and 1980s, researchers at the National Institutes of Health took over the vaccine's development, adding technology and sponsoring a series of patient trials to study its safety, effectiveness and dosage.

In 1995, Aviron licensed the vaccine from the University of Michigan with plans to bring it to market. It reformulated the vaccine as a nasal spray and funded the large clinical trials needed to prove its safety and effectiveness to government regulators. Studies involving about 24,000 patients found the vaccine to be more than 90 percent effective in preventing influenza as well as flu-related ear infections.

Researchers believe FluMist's approval could lead to more widespread vaccination, which could reduce flu epidemics. The current needle-delivered vaccine is approved for almost all people above 6 months of age, but most opt not to get the annual injection. Most children do not receive flu shots, even though they are most likely to catch and spread the flu.

"There are a lot of people who refuse to take influenza vaccine because they don't like needles," said Robert B. Belshe, director of the Center for Vaccine Development at the St. Louis University School of Medicine. He has conducted clinical trials of various versions of FluMist over the past two decades.

Many pediatricians, flu experts and Aviron investors were disappointed in July when an FDA panel recommended against FluMist's approval. Among its concerns, the panel members were worried about a possible link between the vaccine and pneumonia and wanted more data about its impact on asthma patients.

Meanwhile, MedImmune was searching for a second act to follow Synagis's success. Worldwide Synagis sales reached $516 million last year, up 21 percent from 2000, but some analysts believe the antibody-based drug will soon reach its market potential. The company has several experimental drugs undergoing patient testing, but they are years away from hitting the marketplace, and their success is far from assured.
In December, as a wave of mergers swept through the biotech industry, MedImmune announced it would acquire Aviron. Company officials said they saw a large potential market for FluMist, especially among children and teenagers. They set annual FluMist sales goals of $500 million within three years and $1 billion within five years of launch. In January, the company resubmitted its FDA application with additional data to address the FDA's previous concerns.

Many Wall Street analysts believe FluMist will win approval this time for several reasons. They cite the fact that MedImmune founder Wayne T. Hockmeyer was a member of Aviron's board, so he must be confident in FluMist's chances for approval. The company hired a former FDA official who helped review the vaccine. And MedImmune has a good track record with the agency.

"Aviron didn't have the best working relationship with the agency," said Bill Tanner, an analyst at SG Cowen Securities Corp., which does not have a banking relationship with MedImmune. "MedImmune has to at least show they can execute. They have a good working relationship with the FDA."

But not everybody is buying the story. "The idea that Flumist could ever be a $500 million drug is not believable," said David Hines, president of Avalon Research Group Inc., a Boca Raton, Fla., firm that provides research to fund managers including short-sellers -- traders who make money by betting a stock's price will drop. "We question if FluMist could ever receive FDA marketing clearance."

Avalon researchers point to safety issues that were not raised by the FDA panel but could hurt FluMist's chances of approval. One is that the FluMist could be inadvertently transmitted to people who should not be exposed to the vaccine. Another is that a live virus could combine with other viruses to create new viral strains. More clinical trials may be needed to address these issues, which would delay the product's commercial launch.

Unlike experimental drugs for chronic diseases with few treatment options, there is not a pressing need for a new flu vaccine, Avalon researchers said. So FDA officials may not feel compelled to approve FluMist if they believe the risks outweigh the benefits.

Even if it is approved, they doubt FluMist's commercial viability. They question how many people will pay as much as $20 more for a nasal-spray vaccine when the current vaccine works fine. In addition, they say FluMist will be less accessible to the public because the vaccine must be stored at cool temperatures.

"MedImmune has a solution to a problem that doesn't exist," Hines said. "It's too expensive and inconvenient. If it's important to vaccinate children for flu, give them the $10 shot. It's safe and effective, tried and true."
MedImmune believers dismiss these concerns as the worries of naysayers who will benefit from the company's failure. Some say the FDA would have already raised concerns over transmission and genetic recombination if they were problematic. Others say such concerns are legitimate, but will not likely stand in the way of FDA approval.

"No drug is perfectly safe," said Victor Li, who manages a biotech hedge fund at Arlington investment bank Friedman, Billings & Ramsey. His fund holds MedImmune stock. "Driving kills a lot of people, but they still allow people to drive."

Analysts believe there will be plenty of customers willing to pay more to avoid the needle. And they express confidence that MedImmune's FluMist marketing partner, American Home Products Corp., has the expertise and muscle to drive vaccine sales.

Many health experts support FluMist because it would offer doctors another tool to fight influenza and make up for recent shortages of flu vaccine. They say increasing vaccination rates and reducing flu infections could save the nation billions of dollars in health care costs and missed work.

"I believe it's an important drug, particularly for children and the elderly," said John McCamant, editor of the Medical Technology Stock Letter. "Overall, a new flu vaccine has a net economic benefit for us all."

© 2002 The Washington Post Company