MEMPHIS, Tenn. -- By the late 1990s, scientists Karen Slobod and Julia Hurwitz of St. Jude Children's Research Hospital here had an experimental AIDS vaccine on the drawing board unlike any other. It showed great promise in the test tube and in animals such as mice, rabbits and chimpanzees.

But not one of the drug companies St. Jude approached was interested in steering the drug through the costly gantlet of regulatory approval. Fixated on the search for blockbusters, the industry was growing more and more risk-averse.

So the hospital decided to take matters into its own hands. The researchers produced small amounts of the new vaccine and began to test its safety in people. Then St. Jude decided to build its own facility with the aim of taking drugs into small-scale production and through enough testing to make them attractive to a drug company.

In August, St. Jude opened a $40 million drug-production plant, complete with clean rooms and laboratories, airlocks and loading docks. It has the Food and Drug Administration's imprimatur as a "good manufacturing practices," or GMP, facility, which means it has passed inspection for all the strictures and controls needed to handle biological materials without contamination.

Now, St. Jude plans to take drugs through the early stages of clinical trials and then hope to get drug-industry interest in prospects that have made it through those hoops. "If we can show [a compound] works, then we hope a pharmaceutical or biotech firm will pick it up, since we will have taken all the risk out of developing it," says William Evans, the hospital's scientific director.

"De-risking" has become the new buzzword in drug development. A growing number of universities and hospitals are moving beyond basic science and into limited drug development in an attempt to provide companies with compounds that are less likely to stumble on the road to FDA approval.
It's their response to a sense of desperation among many scientists and patient advocates that, despite numerous biomedical discoveries, the number being translated into clinical practice has been declining in recent years. The number of new drugs approved by the FDA fell to 17 in 2002 and had reached 20 by last November for 2003, compared with a 1996 peak of 53.

In August, Stanford University, the nonprofit research institute SRI International in Menlo Park, Calif., and the University of California campuses at San Diego, San Francisco and Berkeley, launched PharmaStart, a consortium intended to accelerate the translation of new compounds from discovery into clinical use. The goal is to do the roughly two years of preclinical lab and animal work needed to establish how the body breaks down a compound and what risks it might pose. After that, it's ready for a request to the FDA to test it on humans.

In 2002, UC San Diego launched TransMed, which acts as a matchmaker between the university's researchers who have leads on promising new drugs -- 28 have submitted proposals so far -- and venture-capital firms.

"With so few biotech start-ups now, many good ideas run out of fuel and never get developed into a new drug," says Edward Holmes, the university's vice chancellor for health sciences. TransMed aims to bridge "the funding gap between the first lab findings and the development and testing of these promising new compounds."

Drug companies these days must pick their shots carefully because drug development is so expensive. After factoring in all the failures, it costs about $800 million to develop a single novel compound into a marketable drug, according to a report this spring from the Tufts Center for the Study of Drug Development.

Consolidation in the pharmaceutical industry also is a factor, forcing big companies to focus on potential top sellers. "The larger the company, the bigger the blockbuster you need ... to support your infrastructure," says Patricia Harsche Weeks, vice president for planning and business development at Philadelphia's Fox Chase Cancer Center and president of the Association of University Technology Managers.

So, while academic and medical centers have been awarded patents for thousands of inventions, including potential new pharmaceuticals, the vast majority fail to find licensees.

St. Jude is in a particularly good position to bring drugs further along the development process because its fund-raising prowess nets some $300 million a year. Small-scale production of the experimental AIDS vaccine, for instance, enough to supply early small-scale clinical trials, is expected to cost a few million dollars. The hospital was founded in 1962 by the late entertainer Danny Thomas to treat children with cancer.

The 64,000-square-foot GMP facility could pay off handsomely for St. Jude. Compounds that have proved their safety and efficacy in clinical trials command much higher licensing fees or royalties, Mr. Kaitin says.

Something that has undergone only preclinical testing, or even the first phase of safety testing, might earn a royalty rate from a commercial partner of about 6%, estimates Steve Harr, a biotech analyst at Morgan Stanley. But compounds that have survived what the FDA calls a Phase II clinical trial, which also tests for efficacy, can bring royalties of 20% to 40%, he says.

When St. Jude's Dr. Hurwitz, an immunologist, and Dr. Slobod, an infectious-disease specialist, had no luck getting drug companies interested in their project, they hired a contract laboratory, which produces...
biological compounds according to scientists’ specifications. The doctors were prepared to spend $1
million (part from a vaccine-development grant made by the National Institutes of Health and part from
the American Lebanese Syrian Associated Charities, St. Jude's fund-raising arm).

Producing a vaccine often requires growing live cells, such as monkey-kidney cells and Chinese-hamster-
ovoary cells, in giant vats called bioreactors. These cells, which are genetically engineered to produce
specific proteins, act as biological factories, churning out the proteins that would be used in a vaccine.

When injected, the proteins train the immune system to attack the virus when the vaccinated person is
exposed to it. In order to provide immunity against the dozens of variants of HIV, the virus that causes
AIDS, the vaccine would contain no fewer than 23 of the outer proteins characteristic of one or another
of the many HIV strains out there.

But the contractors kept flubbing their attempts to coax anything useful out of the ovary cells of Chinese
hamsters. The contract lab couldn't purify the proteins that the Chinese-hamster cells were producing or
run tests to measure those proteins, so St. Jude canceled the contract. "We had been wasting our time," Dr. Hurwitz says.

Other St. Jude researchers had felt that frustration. The hospital's scientists had a successful track record
in medical innovation. St. Jude researchers developed a combination therapy for children with acute
lymphoblastic leukemia that increased survival rates to 80% today from 4% in 1962 when the hospital
opened. Another treatment improved the cure rate for neuroblastoma, the second most common solid
tumor in children, to 59% from 10%. But other potential treatments were stuck on the drawing board.

"We had all this research in place which had evolved to the point of clinical trials, but no one would do
it," says Elaine Tuomanen, head of the Department of Infectious Diseases.

Beginning in 2000, she and other St. Jude officials spent months traveling the country to see the
production facilities at other biomedical institutions. "They were very rare," she says. "There might be a
room or two producing GMP-grade material for the investigator to do something small with," such as
testing a compound's toxicity.

Her initial thought -- that a five- or six-room facility might be sufficient -- was quickly swamped by the
wave of interest among St. Jude's scientists. "It got bigger and bigger," says Dr. Tuomanen.

There was far from universal agreement that building its own GMP facility was the best way for a
biomedical institution to move its bright ideas from workbench to bedside, however.

"We had a lot of people say, 'Don't do it,' " St. Jude's Dr. Evans says. "There's a reason you don't see [a
GMP facility] on every medical-school campus." Scientists aren't necessarily good at running a
successful factory, including record-keeping, repetitive procedures and anything that smacks of cookie-
cutter production rather than cutting-edge discovery.

But because every child receiving cancer treatment at St. Jude is enrolled in an experimental treatment
protocol, or systematic procedure, the hospital already had a large staff with the expertise to run clinical
trials and meet federal regulatory requirements for experimental drugs. To run the factory, it recruited
John Coleman from Dow Chemical Co., where he had set up a small GMP facility.

Any new drug or biological compound, such as a vaccine, that is going to be administered to humans
must be produced in accordance with current good manufacturing practices, which are intended to ensure
uniformity, quality, purity and strength, notes Nick Buhay, a consumer-safety officer with the FDA. To
meet GMP requirements, the St. Jude facility quarantines all biological material that comes in -- viruses,
cell lines, bacteria. A cell line is a population of genetically identical cells, such as kidney or liver, grown
in a glass dish.

Only filtered air reaches the labs. Air locks and double doors keep pathogens from entering or escaping; no electrical outlets penetrate the outside walls, which could create an entry or escape route for microorganisms. Walls are covered with five layers of epoxy so that if they're accidentally hit by a rolling lab cart they flex but don't crack.

The facility's 15 suites are fully booked with St. Jude's own projects for the next two years. In the early planning stages are production of: a monoclonal antibody for treating the pediatric brain cancer called neuroblastoma; a protein that would target leukemia; and gene therapy for hemophilia. The hospital has no plan to turn the GMP facility into a contract lab or lease space to other institutions.

Although it has far to go before proving itself, the facility already is attracting intense interest from other institutions. A university licensing executive who recently attended a meeting with counterparts at high-powered research schools, says, "Everyone said, 'That's what we need to be doing.' "

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