

BIOTECH

REPORT

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Fail Fast, Win Big

WITH A SUDDEN BURST OF 10,000 PROMISING NEW DRUG TARGETS, HOW IS A DRUG COMPANY TO CHOOSE? ENTER CURAGEN, LEADER OF A NEW FIELD: INTEGRATED ANNOTATION.

When it comes to biotech scandal, ImClone is small potatoes. Ever hear of Chemex or Interferon Sciences or Envirogen, Inc. or Morphogenesis? Probably not, unless you were unfortunate enough to invest in companies like these in the early 90s, in which case you will have a hard time forgetting. Remember David Blech? To some, David Blech was a financial wizard, conjuring capital for a slew of small biotech firms. Wizard or con artist?

I watched D. Blech & Co.'s final days from my investment bank's trading floor, as chaos reigned in the market for the small biotech companies that Blech had created. I heard that one senior executive from a major brokerage practically pounded D. Blech & Co.'s door down, demanding payment for trades Blech had made but not settled. Before it was over, the supreme huckster reportedly stood sobbing in his brokerage firm's trading room, and soon thereafter, checked himself into a Manhattan hospital for a few days' rest.

The Blech companies were under so much pressure to show results (i.e. get drugs into clinical trials) that some scanted basic research and rushed miserable chemicals into trials. Even a decade later, few of the companies Blech promoted and financed have produced any really novel commercial products.

Today, many young companies are again seeing unnatural pressure from investors to advance compounds to clinic much too quickly. Wall Street values biotech companies largely on the latest result of the latest phase of a particular clinical trial. Good news in phase 2? Hopes blow sky-high and so do stock prices. The Street's valuation model assumes that success in drug discovery is essentially random. The more compounds in trial, the more potential winners down the road. And so I see lots of even so-called in silico companies trying to transition



Dr. Scott Gottlieb

"Wall Street values biotech companies largely on the latest results of the latest clinical trial. But today, just getting a product into man isn't enough."

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into drug discovery companies too quickly, settling for their first attractive leads before their technology base is complete.

What a shame—especially for investors who may be misled into betting the farm on a bad company with one good product. There are lots of reasons that betting on clinical trials is risky business. For one thing, many biotechnology companies “in-license” the products they have under clinical development anyway, meaning they buy them off their competitors. Even a great new drug can say little about a company’s research capacity and therefore its future productivity.

THE BIG PAYOFF IS A DRUG DISCOVERY PROCESS THAT WEEDS OUT LOSERS EARLY, EVEN BEFORE ENTERING PHASE 1 TRIALS.

But the more important point is this: once it was true that drug discovery was essentially random; the more compounds tested and advanced into trials, the more likely a blockbuster drug down the road. But today, getting a product “into man” (as industry jargon goes) just isn’t enough. The great promise of the biodigital revolution is not simply another great product, but a dramatically more productive drug discovery process. At the heart of this revolution in productivity is a more rational process of choosing which drug targets to pursue and what compounds make it into each phase of clinical trials.

Fail fast, win big

Think about it: right now up to 90 percent of drug candidates in phase 1 trials fail—by some estimates even half of phase 3 candidates fail. From an investment standpoint, the biodigital bonanza will flow not to companies with numerically more winners, but to those with proportionally fewer failures. Better to find out early if a new drug isn’t going to work, rather than after you’ve spent \$300 million on a phase 3 clinical trial. The big payoff is a drug discovery process that weeds out losers earlier, ideally even before entering phase 1 trials. Fail fast, fail cheap, win big.

The need for increased productivity in drug discovery has never been greater. In order to sustain the industry’s historical earnings’ growth of about 10 percent, drug companies need to launch 3 to 5 new drugs annually, each with a sales potential of at least \$300 million per year. That translates into more than 200 new targets entering discovery each year.

Meanwhile, as the number of new potential targets increases, data-rich but knowledge-poor companies face a fundamental difficulty: prioritization. For the last 50 years, the pharmaceutical industry has mined the same 500 molecular targets for drugs. (The drug target is the particular place in the chain of biological interaction that a drug candidate attempts to alter so as to halt or reverse disease.) The same old 500 plan had lots of disadvantages, including increasing drug resistance [See *GBR*, December, 2001], but one great advantage: companies knew an enormous amount about each potential target, including how these targets worked, what happens when they are turned on and off, and likely side effects compounds aiming at this target might unleash. Now suddenly, thanks to an explosion in genomic and proteomics research, the universe of potential drug targets has abruptly expanded from the same old 500 to 10,000. The good news is lots of promising new drug targets—the bad news is they are all targets about which drug companies know relatively little. Which leads should they pursue?

Data to Knowledge

For companies this is not an academic exercise: it takes about 15 years and \$800 million to bring a new chemical entity to market as a drug, in large part due to the high failure rate of clinical trials. A company with one promising compound in phase 1 trials has a 10 percent chance of producing a profitable product years down the road. But a company that finds a way to reduce its drug failure rate—to make 30 or 40 percent

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or more of its candidates succeed—creates not just a marketable product, but a hugely profitable ongoing pipeline of products.

Most genomics companies are sitting on a wealth of information, but few of them know how to make the best use of the intellectual property they've mined from the genome. And so a whole new industry has been created of post-genomics companies pursuing *integrated annotation*, sifting available information about genomic targets to figure out which are more likely to lead to good drugs.

In this new field of integrated annotation, **CuraGen** Corp [CRGN] of New Haven is a leader. Most post-genomic companies are built around just one *in silico* tool. **CuraGen's** uses four different drug discovery tools integrated under an internet-enabled bioinformatics system that allows researchers to share information gleaned in real time. For each potential drug target, **CuraGen** applies an eight-step identification and validation process to provide a maximum amount of information relating to the drug or drug target. It is called GeneScape.

GeneScape

Thanks to GeneScape, **CuraGen** can divine exactly what promising drug targets do, what proteins genes produce, what systems these proteins turn on and off, what chemical compounds are therefore most likely to work where it really counts—outside the lab and inside human beings—what side effects or problems in absorption may occur, and what snip markers can be used to track variations in drug efficacy in different patients. GeneScape transforms drug development from a linear process (where knowledge is laboriously gathered in separate steps) to an iterative process (where data is gathered and shared simultaneously). Technologies that allow researchers to escape the linear trap confer an enormous information advantage.

Walk into a conventional company and you can see the information bottleneck: researchers huddled in discrete areas, each playing with their own technologies and talking to each other (if at all) only after their experiments are finished. Data discoveries made by one group of researchers only rarely and periodically inform what's going on down the hall. Information, in other words, gets wasted. And so does time and money.

At most companies identifying drug targets, establishing compound efficacy, and investigating possible side effects are laboriously separate processes: step 1 might be determining all the proteins for which a gene

codes; step 2 may determine whether the compound that disables a particular gene product will be absorbed well in the human body, and step 3 may involve testing the compound's toxicity to the liver. Success in 1 step says nothing about the likelihood of failure in step 2.

But **CuraGen's** GeneScape allows researchers to consider each question simultaneously at every point in its drug discovery program. Each time researchers pursue a new lead or modify an existing compound, they can consider all the consequences of making a particular choice for efficacy, absorption, and toxicity. When researchers understand how a compound works at the molecular level, they can also make intelligent guesses on how it may be absorbed in humans and what kind of side effects may be expected down the road.

COMPANIES THAT ESCAPE THE LINEAR TRAP REAP AN ENORMOUS INFORMATION ADVANTAGE

CuraGen's entire laboratory is computer-operated. Researchers run wet-lab experiments by keying into their computers, picking which experiments they would like to run from a menu of options: sophisticated lab robots do the experiments rather than an expensive, slow army of Ph.D.s. With GeneScape, no information gets wasted. Insights gleaned in one room are rapidly interpreted and shared to help refine what's going on down the hall.

Downstream Complexity

Genes are simple; molecular biology is hard. DNA is a binary code easily digitized. Complexity arises downstream from the genome in processes that modify proteins and in the variety of protein interactions that change under different cellular conditions and stages of development. Understanding the function of genes and gene products involves multilevel modeling of a complex information chain.

The first link is DNA, which contains all of the hereditary information needed to construct a cell or maintain cellular function. But DNA is stationary, confined to the nucleus. How to get the right data to the right place? DNA is first copied (transcribed) into messenger RNA (*mRNA*). In turn, mRNA travels to protein-manufacturing facilities called *ribosomes*. Ribosomes create the various proteins that perform the bulk of biological functions.

Want a potentially good molecular target for a drug? Locate a gene that seems to be correlated to a particular disease, say hypertension or heart disease. But that is only the first baby step. Drugs do not aim at DNA:

CURAGEN'S TECHNOLOGY PLATFORM CAN DISCOVER DNA SEQUENCES NO ONE HAS EVER THOUGHT TO TRY BEFORE

they almost always try to affect proteins. Finding a good drug target requires identifying the proteins for which genes code and then uncovering the effect in the body of turning particular protein-manufacturing messages on or off. Identify what proteins do, and you have a shot at finding compounds that stimulate or block their production, depending upon the role they play in disease development.

Not all systems are created equal. **CuraGen's** technology platform, for example, can discover DNA sequences (and therefore molecular drug targets) no one has ever thought to try before. Affymetrix Inc.'s [AFFX] gene chip system, by contrast, can't uncover

novel genes. Why not? Well, the system works by embedding a particular DNA sequence on the chip and then testing it against sample tissue. [See *GBR*, October 2001]. That means this design can only test fixed, known DNA sequences to find possible disease involvement. Before a researcher can test whether a gene has any affect on a disease, he must already know the DNA sequence he wants embedded in the chip. **CuraGen's** expression profiling system by contrast allows researchers to roam the whole human genome, spotting genes that are expressed differently in diseased and healthy tissue. (**Human Genome Sciences** [HGSI] takes a different but equally powerful approach to mining the genome that is likely to produce equally valuable but different hits.) [See *GBR*, November 2001].

SeqCalling, et al.

Among the tools **CuraGen** integrates into GeneScape is a gene-sequencing platform called SeqCalling, a bioinformatics tool that allows **CuraGen** to rapidly store and retrieve all the gene-sequence data they generate. SeqCalling permits researchers to make comparisons easily between DNA

Update: Vertex Pharmaceuticals

I used this year's Biotechnology Industry Organization's CEO & Investor Conference at the Waldorf-Astoria to spend quality time with **Vertex Pharmaceuticals** [VRTX] CEO Josh Boger. (See *GBR* Special Report "Medicine Meets Microchip").

Over pasta and iced tea, Josh told me about ambitious 2002 goals: to complete a phase 3 trial and file a new drug application on its newest protease inhibitor VX-175 for the treatment of HIV; a phase 2 study for its drug Pralnacasan used in treating rheumatoid arthritis (as well as beginning trials for other indications); and preclinical development of the first protease inhibitor for hepatitis C, dubbed VX-950. **Vertex** also plans to begin clinical trials with second-generation inflammation inhibitors

VX-702 and VX-850 and enter a phase 2 study with VX-148 for treating autoimmune diseases.

I was struck not just by the impressive list, but by the way these new candidates cluster. **Vertex** has long had a strategy of developing expertise in drugs directed at targets that are structurally related: phosphatases, kinases, and proteases, among others. The groundwork laid in thoroughly understanding new molecular targets is beginning to pay off in whole classes of new drugs. Take protease inhibitors, for instance—best known for dramatically lowering death rates from HIV.

But **Vertex** has also developed protease inhibitors for some of the other more difficult targets known to exist, including a drug targeting HCV protease, an enzyme involved in hepatitis C viral replication, a new inhibitor of the caspase subfamily of proteases (involved in *apoptosis* or

generated from sick patients and healthy controls. For the next step, finding the function of the proteins these genes code for, **CuraGen** uses a platform called PathCalling that uncovers the cellular pathways causing disease and identifies the molecular targets at which drugs can be aimed. **CuraGen**'s tool called SNPCalling characterizes *single nucleotide polymorphisms*, or *snips*. Snips can be used to mine for genes related to a disease, find gene markers that can be used to design clinical trials that target people most likely to respond to a drug, and design diagnostic tests to predict which people are most likely to benefit (or experience side effects) from a new medicine. [See *GBR*, January 2002].

By themselves, any one of **CuraGen**'s tools may be no better than any other company's: **CuraGen**'s key technology advantage is integration. If the question is which drug target is best or which drug compound is likely to succeed, no single technology can provide the best answers. Companies that grew up around a single tool, such as a unique way to identify the protein products of genes, are now trying hastily to integrate other technologies for annotating genomic targets. **CuraGen** has been doing that from the very start; they've inte-

grated their entire broad base of tools through a single operating system and database, with multiple users sharing the output from each technology. If researchers glean something useful from one platform, they can use it to refine a test for toxicity at the same time they're running another platform, making maximal use of the information they're generating.

GeneCalling

A fourth platform is a *differential display* tool, widely used in the gene annotation industry that **CuraGen** dubs GeneCalling. In this method of expression profiling, expressed mRNAs are used as templates to produce copies of the original DNA, called doublestranded *cDNA*. The most significant advantages of GeneCalling are its simplicity and the possibility of detecting virtually all expressed mRNAs, using only very small amounts of total RNA. The technology's ability to analyze rapidly the expression patterns of several hundred genes in a single experiment makes its differential display one of the best methods for uncovering novel genes.

CuraGen's GeneCalling technique is one of the most sophisticated and successful differential display

cell self-destruction), as well as a novel inhibitor of HIV protease. Becoming an expert in protease inhibitors, it turns out, pays dividends across a variety of diseases.

Vertex's VX-950, a protease inhibitor for hepatitis C (with 200 million sufferers worldwide) has real blockbuster potential. Expect in-man studies as early as 2003, which would make **Vertex** first-in-line to develop a successful hepatitis C protease inhibitor. As a direct antiviral, VX-950 has the potential to be a highly potent drug, even a monotherapy—a single pill that will eradicate the virus.

One of **Vertex**'s latest and most interesting entries? A protease inhibitor for Alzheimer's. The characteristic brain plaques found in Alzheimer's (beta amyloids) are made by chopping up a larger molecule, amyloid precursor protein (APP), with enzymes called secretase. Since beta secretase is involved in making APP, scien-

tists predict that drugs blocking its action will reduce the brain's beta amyloid burden. If amyloid plaques cause Alzheimer's, then blocking beta secretase (also known simply as BACE) may slow progression of the disease. **Vertex** is designing novel medicinal chemistry to inhibit BACE and hopes to have a compound in pre-clinical development next year.

So what happened to **Vertex**'s stock price? Partly, the stock is still hungover from its disappointing clinical trial results with a rheumatoid arthritis drug and an earlier drug for hepatitis C (typical Street wisdom). Mostly, it has tracked the biotech market's slow erosion over the last three months.

Like **CuraGen** (profiled in this issue), **Vertex** is a long-term winner with a lot of short-term upside. Under \$30 it's a steal. **B**

technologies adapted for *high-sample throughput* (which is a fancy word for quickly generating useful leads from genomic data). GeneCalling has been used by many of **CuraGen**'s clients and is a validated and reliable mRNA profiling technology, examining mRNA production to spot differences between the

YOU CAN BUY CURAGEN'S INTELLECTUAL PROPERTY CHEAP AND RIDE IT UPWARD OVER THE NEXT FIVE YEARS

gene expression of normal and diseased tissue. It can also identify differences between patients who have received a drug and untreated controls. Thus, unlike many competing companies, **CuraGen** is able to identify drug-specific gene responses efficiently. GeneCalling has a low false-positive rate along with high sensitivity in detecting even the smallest gene expression changes. Why does this matter? False positives are hits that are not really hits. Weeding them out increases the likelihood that the drug leads a company pursues will succeed.

CuraGen Collaborations

These tools are not only powerful boosts to **CuraGen**'s drug development, but marketable products in their own right. Challenged by rapid technological changes and innovations, combined with the pressure to reduce costs, speed development timelines and increase productivity, the pharmaceutical industry has never been under greater pressure to seek more effective drug discovery strategies. An important route for drugmakers in overcoming these challenges will be access to biotechnology's developing expertise and comprehensive cost-cutting solutions, which are increasingly dominating the paths to new drug discovery and new treatments. Drugmakers are becoming increasingly dependent on strong, long-term alliances with leading biotechnology companies in order to grow their pipelines. **CuraGen** has the skills to pursue such collaborations, developing bioinformatic tools for its own use and then marketing them to Big Pharma as well. In addition to collaborations aimed at developing its own pipeline, **CuraGen** has deals with GlaxoSmithKline PLC [GSK] and Roche [RHHBY] to help those drug giants prioritize their own drug leads, at the same time developing snip markers useful in future clinical trials. [See *GBR*, January 2002].

As part of its \$1.4 billion drug discovery alliance with

Bayer AG [BAY], signed in January of last year, **CuraGen** is developing a database of gene-based markers that will help Bayer researchers predict the potential toxicity of drug candidates. Bayer's choice of **CuraGen**'s target validation platform only confirms my own high opinion of the technology's use in the crucial process of prioritizing drug leads, including those preclinical stage drug targets supplied by Bayer's other drug discovery partners.

Liver toxicity generates some of the most expensive, late-stage failures of all—after drugs have already been FDA-approved and marketed. Remember the popular drugs Troglitazone for diabetes, Lotronex for irritable bowel syndrome, and Trovan for infections? Each was pulled from the market after they were found to cause liver failure in a tiny fraction of patients. Liver injury is the principal safety reason for terminating clinical trials of drugs and withdrawing them after they've been marketed. The liver is the organ where most drugs are metabolized: **CuraGen**'s computational models of how the liver works will permit earlier detection of toxic compounds and may even allow structure-activity relationship modeling to tailor formerly failed compounds into viable drug leads.

Naysayers argue that technology, like predictive toxicology, is a mixed blessing for drug companies. They say that liability lawyers would be quick to use the data to make companies liable for these late-stage failures. It's true: given the political environment, you don't necessarily want a more sensitive way to look for poisons. Take the British arm of Friends of the Earth, which issued a report earlier this year called "Crisis in Chemicals," in which it argued that genetic studies would make it easier to link a chemical to a disease, increasing the chances of winning liability lawsuits. But the costs of waiting for drugs to fail in clinical trials—much less get pulled from the market—are so high that the industry can't ignore tools that will make it easier to spot problems early. Meanwhile, like it or not, once liability lawyers discover that the technology exists to predict even rare side effects, the pressures of potential litigation will drive even more pharma firms to companies like **CuraGen**.

CuraGen began life as a research-driven company, cracking the human genetic code to find promising targets for new drugs. But rather than settling for selling this information, **CuraGen** followed the path laid out by Millennium Pharmaceuticals [MLNM] and Human Genome Sciences [HGSI], building itself into a drug-maker in its own right. Under its deal with Bayer, **CuraGen** will provide 80 genetic targets for potential

drugs to treat obesity and diabetes, which together account for \$98 billion in healthcare spending in the United States alone. And both companies will share in developing these potential drugs to the tune of some \$1.3 billion over 15 years, with Bayer paying 56 percent of the cost and **CuraGen** the rest.

Unlike most previous biotech-drug company deals, **CuraGen** will not get the usual 10 percent to 20 percent royalty on future drug sales, but will be a full marketing partner, with 44 percent share of the profit, effectively making the deal a joint venture with Bayer. The two companies recently announced that they have finished screening against the first four targets and have so far selected a total of 31 of the 80 targets promised to Bayer during the next five years. **CuraGen**'s collaborations are ideal because they allow it to continue focusing on what it does best, finding and validating drug leads, leaving the actual development of the drugs themselves to others with expertise in these fields. In each case, **CuraGen** will send their partners those genomic targets that they believe will be best adapted to their partners' particular drug technology. Targets that are amenable to antibodies (receptors on the surfaces of cells) will be shipped to a partner like Abgenix (ABGX), while those that are best reached by small molecules (intracellular targets) will be sent to Bayer. **CuraGen**, like Human Genome Sciences, retains protein-based drugs to be developed in-house. **CuraGen** rents the application to Big Pharma but retains the core technology for its own account.

Along with gene discovery and gene expression tools, **CuraGen** also has expertise in snip discovery and deciphering protein-protein interactions. When **CuraGen** takes a product into the clinic, it will have the genetic markers to help predict problems and to identify clinical opportunities such as which patients will benefit most from a drug.

In the last issue of the *Gilder Biotechnology Report*, I point out that **MDS Proteomics** has one of the single best strategies for deciphering protein-protein interactions, even better than **CuraGen**'s. But with **CuraGen**, it's not simply one tool that is technologically superior; it's their combined expertise in the essential components of converting genes into drugs and their ability to integrate important tools that makes this company a standout. **CuraGen** is just beginning life as a drug discovery shop: you can buy its intellectual property cheaply and ride it upward as **CuraGen** grows its pipeline over the next five years.

Look at the numbers. **CuraGen** has a market cap of about \$750 million: \$508 million in cash and about \$150 million in debt. That gives the company's technology a value of about \$390 million. But look at what the company is up to. It has a \$1.4 billion deal with Bayer and has already delivered 100 drug targets to Hoffman-La Roche. Its overall body of drug targets includes 120 proteins and 191 monoclonal antibodies, among others. And it plans to move two drugs into the clinic this year. Compare what **CuraGen** is doing to a company like ImClone, which soared to *more* than \$4 billion in market value by moving a single monoclonal antibody into advanced clinical trials. Just 1 out of **CuraGen**'s 191 monoclonal antibodies could put **CuraGen** where ImClone was before it tripped and fell by failing to properly document its trial (See *GBR* January 2002). That's a pretty good risk return. **CuraGen** has also filed for patents on more than 2,000 pharmaceutically tractable genes.

THANKS TO AN UNPRECEDENTED VALIDATION PROCESS CURAGEN'S FUTURE CLINICAL TRIALS WILL NOT BE EXERCISES IN FAILURES

CuraGen's work has been validated by about ten published scientific papers in 2001 alone. Two publications describe particularly interesting novel drug targets identified by **CuraGen** scientists that may play crucial roles in the development of cancer. They've been able to construct a substantial preclinical pipeline encompassing four therapeutic franchise areas: oncology, inflammation, central nervous system disorders, and metabolic diseases. Currently, an estimated 37 percent of **CuraGen**'s validated targets relate to metabolic disorders, 40 percent to oncology, 18 percent to inflammation, and the remaining 5 percent to CNS (central nervous system) disorders, including multiple sclerosis, Alzheimer's disease, pain disorders, schizophrenia, and depression. This latter group is **CuraGen**'s youngest program, so they're still at the target validation stage. These are large market opportunities and likely suspects for a genomics-enabled discovery platform, since they are all believed to have a genetic component.

And there's only upside from here on out. While other biotechnology companies have products in clinical trials that spell potential pitfalls if trials fail, **CuraGen** will report only good, market-moving news over the next two years as it advances products

BIOTECH COMPANIES

Company	Technology Leadership	Reference Date	Reference Price	2/28/02 Price	52-Week Range	Market Cap
Vertex (VRTX)	Rational Drug Design	9/17/01	28.60	21.81	15.50 - 56.75	1.64B
Human Genome Sciences (HGS)	Cellular Signaling	10/26/01	43.97	20.52	19.76 - 77.00	2.62B
Nanogen (NGEN)	BioChips	10/2/01	4.95	4.14	3.00 - 10.60	89.5M
Gilead Sciences (GILD)	Rational Drug Design	12/05/01	67.72	70.46	26.88 - 73.67	6.76B
Quorex (none*)	Rational Drug Design	12/05/01				
Sequenom (SQNM)	Pharmacogenomics	1/09/02	9.00	5.68	5.65 - 18.70	212.2M
MDS Proteomics (none*)	Proteomics	2/05/02				
CuraGen (CRGN)	Cellular Signalling	3/13/02	17.67		13.87 - 41.34	860.4M

* Pre-IPO startup companies.

NOTE: This list of Gilder Biotech companies is not a model portfolio. It is a list of technologies in the Gilder biotech paradigm and of companies that lead in their applications. Companies appear on this list only for their technology leadership, without consideration of their current share price or the appropriate timing of an investment decision. The presence of a company on the list is not a recommendation to buy shares at the current price. Reference Price is the company's closing share price on the Reference Date, the day the company was added to the table, typically the last trading day of the month prior to publication. The author and other Gilder Publishing, LLC staff may hold positions in some or all of the companies listed or discussed in the issue.

out of the laboratory and into the clinic. **CuraGen** told us it expects to file two investigational new drug (INDs) applications this year on biologics. The first is expected to be for ulcerative colitis (a chronic disease affecting 150,000 Americans). The second one is as yet a company secret. **CuraGen** also has big opportunities to strike new collaborations. Essentially, the kind of deals **CuraGen** has struck with Bayer AG allows it to pursue everything outside the obesity and diabetes market on its own or with another pharmaceutical company.

Using traditional methods, it takes 6 to 12 years to transition from target discovery to clinical development. Only in the past two years has the right mix of tools, technologies, and critical mass of high-quality data become available to break through barriers in the drug discovery industry and dramatically speed discovery and development. In the new data-rich, knowledge-poor post-

genomics world, the winning companies will be those that acquire the in silico expertise to increase productivity in the drug discovery process, sign up credible partners, and achieve broad acceptance of their technologies.

Because the drug leads it ultimately chooses have already passed an unprecedented validation process of empirical and computational tests, **CuraGen's** future clinical trials will not be exercises in failures. For the new generation of drugs created by technological leaps such as **CuraGen's** GeneScope, clinical trials—the ultimate wet lab—will merely confirm efficacy and safety already established in preclinical tests. Fail fast, fail early, win big. **CuraGen** looks like a big winner.

Scott Gottlieb
March 13, 2002

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