teams Reprogenesis and Creative already have, Platika says, and years for Reprogenesis and Creative to build a discovery engine like Ontogeny's. The three companies fit together, he says, like "pieces of a jigsaw puzzle," and the net effect of merging will allow each group to "leapfrog" its technology two to three years into the future.

Nevertheless, it is Platika with his background in discovery who will become Curis' president and CEO, while Tarnow and Dan Omstead, president and CEO of Reprogenesis, will depart once the merger is complete.

Although all three companies focus on regenerative medicine, there is little overlap in their research, says Omstead. Reprogenesis holds exclusive rights to a product called Chondrogel, a drug for a pediatric urological disorder called vesicoureteral reflux that is currently in pivotal phase III clinical trials. It also has several patents related to tissue engineering and has products in the areas of urology, cardiovascular biology, and reconstructive surgery in its clinical and preclinical pipeline. Ontogeny, on the other hand, has rights to the hedgehog family of molecules, which control key stages of embryonic development, and also holds patents in research related to neurological disorders, dermatological disorders, and diabetes. And Creative BioMolecules' OP-1 family of implants for orthopedic reconstruction—being co-developed with medical product company Stryker Corp. (Kalamazoo, MI)—is currently undergoing regulatory review in the US, Europe, and Australia and could be approved sometime this year.

Platika says the combined intellectual property of the three companies will create a "formidable entity" that will give Curis the freedom to operate in many areas of what is an increasingly popular field. He sees the competition as established companies like Human Genome Sciences (HGS; Rockville, MD) and Genentech (S. San Francisco, CA), which are moving into areas of regenerative medicine, and notes that pharmaceutical giant Eli Lilly (Indianapolis, IN) has a major initiative in the field.

Following the merger, which is subject to shareholder approval and expected to take place by June, shareholders of Creative BioMolecules will hold 43% of Curis, receiving 3 shares of Curis for every 10 of Creative. Ontogeny and Reprogenesis shareholders will hold 38% and 19%, respectively. For now, Curis will have $70 million in cash reserves, enough to keep the company going for two years, Platika says.

Platika plans to double Curis' 150 employees within a few years, paying particular attention to clinical development and sales and marketing. None of the three companies currently has a marketing team in place, but Platika believes Curis has time to build one before its first self-marketed product—probably Chondrogel, Reprogenesis' urology drug—receives approval. For larger-market products, such as a compound that may activate hair growth, or potential drugs for diabetes or stroke, he says partnering with a larger pharmaceutical or consumer products company that has a worldwide sales force would still be the way to go.

Julie Grisham

Scrutiny of gene therapy broadens, intensifies

Officials at the US Food and Drug Administration (FDA; Rockville, MD) and National Institutes of Health (NIH; Bethesda, MD) have adopted several measures to improve the safety of participants in gene therapy clinical trials. Earlier in the month, members of the National Bioethics Advisory Commission (NBAC; Rockville, MD) said that they would include the safety of gene therapy trial participants in their comprehensive investigation of research involving human subjects.

In March, FDA officials issued a statement requiring all sponsors of gene therapy products to submit substantial, additional information to the agency as a way of improving safety procedures. This request extends not only to clinical trials but also to animal testing results and to materials that may have been intended for use in clinical trials but for one reason or another were not so used. The FDA also reminds sponsors to confirm that data from animal safety trials are submitted to the agency, with special regard to those studies that "suggest significant clinical risk."

However, the toughest new requirements from FDA focus on clinical trials—particularly on ensuring "adequate oversight" for this phase of product testing. Agency officials will review the safety monitoring plans of product sponsors, and officials promise to "see modifications as warranted to improve the quality…." FDA also warns that it will conduct surveillance and "for cause" unannounced inspections of clinical trials. In the same vein, NIH will undertake "not for cause" site visits to NIH-supported institutes with ongoing clinical trials to determine how they are being conducted and whether they fully comply with NIH guidelines.

"Clinical trial monitoring and responsible reporting must be taken seriously by all parties involved in gene therapy trials," says FDA Commissioner Jane Henney. "Our plan will help restore the confidence in the trials' integrity that is essential if gene therapy studies are to be able to fulfill their potential."

The second new component of oversight from FDA and NIH entails convening a regular series of "Gene Transfer Safety" symposia to be held about four times per year. These public meetings will provide "critical forums for the sharing and analysis of medical and scientific data" from gene transfer and gene therapy research efforts. As part of this series, the two federal agencies indicate that they will provide support to professional organizations and academic centers interested in holding such conferences.

Several members of Congress who have been critical of FDA and NIH over their handling of gene therapy oversight praise their recent reform measures but also suggest that they do not go far enough. For instance, Senator Bill Frist (R-TN), who chairs the Senate Health, Education, Labor, and Pensions Committee Public Health Subcommittee, says that he still plans to hold additional hearings looking into gene therapy-related issues. And Senator Edward Kennedy (D-MA) not only has issued a series of specific recommendations for changes at both FDA and NIH, but also says that legislation may be required to restore public confidence in federal oversight of this research.

Meanwhile, NBAC will not add another layer of day-to-day oversight, nor is it planning to preempt ongoing FDA and NIH investigations of gene therapy clinical trials, according to NBAC Chair Harold Shapiro, who is president of Princeton University (Princeton, NJ). Noting that the commission is itself "not an operating agency," he says that its members nonetheless may develop additional guidelines for gene therapy clinical research "to enable the agencies to work more effectively together."

Several NBAC members point to the need for more resources for oversight of gene therapy and other clinical research at both the federal and local levels, while others cite increasingly complex public–private funding arrangements as an important complicating factor in this arena. More significantly, NBAC members assert that an important principle that they first embraced in 1997—namely that human subjects in such trials deserve careful protection regardless of whether the federal government or sponsors in the private sector are paying for that research—should be applied to gene therapy.

Jeffrey L. Fox