

## Biopharm Business Development

# Biotech Innovation And Access To Capital In An Era Of Reform

By Gail Dutton

**I**n an era of healthcare reform, legislative initiatives and incentives are countering each other, creating a high level of uncertainty that is causing investors to watch from the sidelines and life sciences companies to seek safer, more assured business strategies. “We live in a policy bipolar

world,” Alan Eisenberg, executive VP, emerging companies and business development at BIO, acknowledges, speaking at the BIO-Europe International Partnering Conference in Munich last November. Although governments throughout the world have established incentives to spur innovation, they also have enacted other legislation that stymies investment and makes due diligence and drug development “vastly more difficult,” according to Gary Geipel, Ph.D., director of corporate affairs, Lilly Deutschland.

In the United States, for example, although healthcare reform legislation increased grants and incentives, those bills also called for pharmaceutical contributions, comparative effectiveness reviews, and independent advisory boards that increase risks and actually penalize successful programs. “There is an odd juxtaposition of incentives and interests that are industry-based,” Eisenberg points out.

In Germany, a moratorium recently was placed on price increases for branded drugs until the end of 2013. About the same time, the Bundestag (the lower unicameral house of the parliament of Germany) increased mandatory rebates from 6% to 16%. More recently, to receive the best pricing, all new products launched on or after Jan. 1, 2011, must pass an assessment of added medical benefit within three months of their launch date. Otherwise, “they are consigned to reference pricing, which effectively condemns

them to extinction,” Geipel says. That price will hold for 12 months, when they become subject to rebate negotiations. “This is a significant set of developments that will have spillover effect elsewhere in the world,” Geipel elaborates. Vaughn Kailian, managing director MPM Capital, agrees. “Look at Europe to see what will hit the United States. Whatever happens here will eventually happen in the United States,” he predicts.

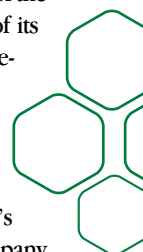
### LOW-RISK DEVELOPMENT

In the midst of such changes, early-stage companies are protecting themselves. Kailian advises moving to “areas of greater certainty — areas not regulated by the FDA, or that are more consistent with policies, or to ‘me-too’ drugs,” if the uncertainty continues. “Nutraceuticals,” he adds, “are not a trivial area.” Nutraceuticals are one relatively low-risk avenue, but companies presenting at the BIO-Europe partnering event highlighted other strategies. A noticeable number of those companies are creating a cash flow for all or part of their developmental pipeline by accessing government programs that promote the development of orphan drugs, or by developing drug combinations that can be quickly approved, or by improving the delivery mechanism, efficacy, or side effects profile of a drug just coming off patent.

“TheraVida, Inc., in San Mateo, CA, for

example, focuses on improving the clinical benefits of existing drugs, primarily by reducing dose-limiting side effects and then increasing efficacy through higher doses,” according to Roger Flugel, Ph.D., CEO. The approach combines two approved drugs for a lower-risk, high-return approach, he says. The new drug application is filed through the FDA’s 505(b)(2) regulatory pathway. TheraVida is initially targeting antimuscarinic therapies, which are used to treat incontinence. The approved drugs relax smooth muscle and reduce the production of saliva, sweat, and gastrointestinal juices but, unfortunately, also cause pronounced dry mouth. He notes that it’s a \$2.5 billion market, and all the existing drugs have dose-limiting side effects that result in a 20% percent compliance rate. By eliminating the side effects, he expects to increase compliance and efficacy.

Galantos Pharma GmbH in Mainz, Germany, is targeting Alzheimer’s disease and dementia, using a prodrug version of the approved therapy, galantamine. Because of its prodrug status, reduced clinical requirements are expected. Existing therapies are at the limit of their effectiveness. Galantos’ prodrug version eliminates side effects and is orally administered. As there has been no new Alzheimer’s drug in the market since 2002, the company considers this a low-risk deal with a good therapeutic window. It received 4.4 million (euros) round C influx of capital from





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groups of investors that included the German state bank, the Ministry for Education and Research, the High Tech Fund, and two other German venture funds.

Twelve-year-old PTC Therapeutics in South Plainfield, NJ, recently won a \$1.6 million FDA Orphan Drug Grant to advance ataluren, a protein replacement therapy for patients with nonsense mutation cystic fibrosis. As another part of its strategy, PTC also has developed a screening technology to identify small molecules that modulate posttranscriptional control mechanisms. It has raised about \$500 million so far from global venture capital, collaborations, and research grants.

Pevion Biotech, in Bern, Switzerland, in contrast, focuses upon novel therapeutics for unmet needs. Although its therapeutic agent is novel, its vivosome delivery platform is already approved, and it generates a robust B cell response. Currently it is developing a therapeutic candida vaccine for women suffering from recurrent vulvovaginal candidiasis. The company has exclusive rights to the key antigen, SAP2, and plans to advance the therapy only through Phase 2 proof-of-concept trials.

Some companies, of course, are targeting potential blockbuster therapeutics. AFFiRiS, in Vienna, is focusing on chronic diseases and unmet needs, developing a synthetic peptide-based vaccine delivered through proprietary platform. “The old economy focused on infectious diseases,” notes Walter Schmidt, Ph.D., CEO of AFFiRiS. “The new economy vaccines focus on chronic diseases.” He estimates the potential market in the billions to tens of billions of euros.

## COLLABORATIONS

These early-stage companies were funded with a combination of government grants, industry collaborations, and venture capital. As funds become scarce, they are turning, increasingly, to collaborations. Big pharma and big biotechs that rarely engaged in collaborations now are seeking them out. AstraZeneca, for example, is increasing its emphasis on partnerships, especially in companion diagnostics for its drug development program, as well as for technologies with utility across the company’s portfolio, according to Cecilia Schott, Pharm.D., business development director for personalized healthcare.

The reason for the partnering, according to Phillippe Groupit, senior VP, business development and corporate licensing at sanofi-aventis, is that “we discovered we had a better probability of success.” That rationale was so great that it led the company to merge research endeavors with collaborators in a way that resulted in sanofi-aventis paying milestone payments and royalties on its own research.

## GOVERNMENT FUNDS

Soft funding in the form of government grants also is growing, but

it often involves relatively small amounts and sometimes comes with strings attached. For example, Kailian notes that the U.S. government gave the life sciences industry \$1 billion in therapeutic research grants, up to a maximum of \$500 million per company for two years. They got four times more applications than expected, so rather than make judgments, they divided the approximately 4,000 projects into \$1 billion. With grants averaging \$244,427 per project, “that’s the therapeutic equivalent of putting a grain of rice in every cup and expecting to feed your population,” Kailian says.

Likewise, Germany, Spain, Switzerland, France, and the United Kingdom, among others, have funds to attract innovative companies, Christian Schneider, Ph.D., managing partner at Vesalius Biocapital, points out. States and regions, as well as some cities

and even local banks, have established venture funds to help finance innovative companies in their regions. “The bad news is that these funds often need to be matched by funds from other venture capital organizations,” he says. Therefore, there is concern that many of the companies that received seed funding will be unable to obtain second round

funding and will not survive.

## UNCERTAINTY

The regulatory restrictions put in place during the past few years, however, outweigh the incentives, Eisenberg admits. “The National Institutes of Health, for example, lists diabetes and obesity as the greatest unmet medical need, but the FDA increases the hurdles of getting diabetes or obesity drugs to market by 50% when they add cardiovascular outcomes to the trials. We’d be happy to do those trials, if we could survive the rest of the hurdles,” Kailian says. “We have a finite amount of resources. The financial supply chain is so thin that anything that goes wrong snaps it. We, as venture capital companies, don’t have enough money to fill the gap.”

“The situation isn’t a lack of capital, it’s a lack of certainty,” Paul Hastings, president and CEO of OncoMed Pharmaceuticals, counters. “Capital will flow into markets where there’s certainty.” Comparative effectiveness, for examples, rewards innovative products. But, Dr. Geipel emphasizes, “Innovation happens in increments, not in revolutions. Our concern in Germany is that incremental innovation is so discounted as to be no longer valued. If we don’t reward incremental innovation, revolutionary innovation won’t be achieved.”

“The task for life sciences companies is to at least have a seat at the table and convince lawmakers not to throw the baby out with the bathwater,” Hastings says. “The more they whittle away at innovation by putting restrictions on us, the less innovative we will become.” ●

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