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MEDICAL DEVICE AND DIAGNOSTIC INDUSTRY

Convergence, Collaboration, Commercialization

Tomorrow's healthcare marketplace will belong to companies that can collaborate effectively to produce next-generation combination products.

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Technology convergence and corporate collaboration are propelling rapid changes in today's medical device industry. Technology convergence is emerging from often disparate disciplines in order to address a wide array of clinical disorders that biologics, devices, or pharmaceuticals cannot resolve independently.

Sidebar: Building a Partnering Strategy

Meanwhile, corporate partnerships are enabling manufacturers to collaborate on such common goals while maximizing the strengths and minimizing the weaknesses of each partner. Partnering across the biotechnology, medical device, and pharmaceutical fields represents an excellent method of creating better, smarter products, and achieving mutual growth.

So far, the results of such collaborations have been exciting, with the result that venture capital funding is pouring into this growing area of medical technology exploration. The concept of medical devices serving as the platform on which to unite disparate technologies in order to provide superior solutions has an irresistible gravity that pulls in savvy investors who are searching for growth opportunities in established markets. As with all such opportunities, however, there are pitfalls and challenges to consider before embarking on a convergent medical technology partnership.

This article provides a roadmap for identifying the opportunities and challenges involved in uniting discrete technologies into a superior solution, with special reference to product development scheduling, final product characteristics, and potential profit. Additionally, it promotes the concept of

collaborative partnerships, which enable a team of corporations to solve complex problems cooperatively, with each member working to its strengths while spreading development risks across the pool of participants. Through such collaborations, products whose technological hurdles would have been beyond the reach of the individual partners acting alone are now feasible. The innovative solutions represented by convergent-technology products are already beginning to displace devices with a long history of use, and rendering obsolete the successes of yesterday.

Before companies start to invest in convergent technologies, however, it is essential that they evaluate the risks associated with such collaborations relative to their internal strengths, weaknesses, and core skills. A risk assessment of this type can best be accomplished through a comprehensive market assessment study and a careful examination of competitors.

Market Potential for Convergent Devices

The growth of the medical device market is being driven by a number of significant factors, including aging populations, faster dissemination of research breakthroughs through improved information technology, and the opening of global markets. Meanwhile, the development of convergent technologies is being spurred by different factors, including rising global wealth, improving healthcare standards, and the gradual expiration of patents for a number of enabling pharmaceuticals. Additionally, areas of healthcare with very great unmet needs that have defied conventional approaches —such as spine-related ailments, heart disease, neurological disorders, and conditions subject to regenerative medicine approaches—still beckon for effective treatments. Estimates of the overall market size for medical devices vary greatly. One recent report estimates that U.S. revenues of publicly traded medical device companies (including conglomerates) totaled approximately $180.5 billion in 2007.[1] Calculations to estimate the size of the global market—including estimated growth of 10% annually—suggest that total worldwide revenues for 2008 may rise to $330 billion or more.[2]

The market for combination products is still quite small by comparison, but many analysts have expressed high hopes for strong growth. By 2009, the global market for convergent products is expected to reach $10 billion, nearly 90% of which will be related to cardiovascular medicine and drug-eluting stents.[3]

Despite pressures on global credit markets, funding for such innovations will remain strong. Venture capital firms in particular recognize the growth opportunities and are increasing their investments. According to *Market Watch* estimates, nearly $3.7 billion was invested in medical device firms in 2007—a 40% increase over the previous record of $2.69 billion for 2006.[4]

Already, products manufactured by integrating biologics, medical devices, and pharmaceuticals into single all-in-one products have emerged as one of the most profitable and lucrative segments of the medical device market. Most large pharmaceutical and medical device companies are investing in the use of convergent technologies to develop combination products. The development of such first-generation combination products as implantable glucose sensors, scaffolds incorporating growth factors to promote bone regeneration, and drug-eluting coronary stents, provides the back-narrative for multi-billion-dollar success stories.

Challenges and Pitfalls

The development of convergent technologies promises significant benefits in terms of clinical efficacy and profitability. But challenges surrounding financial commitment and reward, technology issues, and regulatory affairs remain major factors of concern to medtech companies and venture capitalists alike. Too often, device executives and VC managers see untenable risk in these new business paradigms.

Company reticence to partner with others on convergence projects frequently arises from concern about taking on external risks beyond the company's direct control. In fact, however, the strength of partnering lies in spreading risk across multiple organizations. While each party can manage to its strengths, others can step in to shore up weaknesses. To facilitate such arrangements, the partnering framework should encourage enough openness to ensure that all risks—whether they are financial, technical, or legal—are clearly visible to all of the partners.

Managing financial risk is critical, because any shortcoming or failure has monetary consequences for all parties. Underfunding is the root of most venture failures, underscoring the need for the partners to work together in creating realistic project cost predictions, adequate reserves, staged development plans, and tracked expenses. Additionally, a clear understanding of each partner's financial obligations and each partner's financial rewards is needed from the outset.

Technical risk involves not just the ability to beneficially combine disparate technologies but also to assess whether the convergent device truly offers a superior solution in terms of functionality or cost savings. Beginning with the initial market assessment and external market audit, technical risk needs to be monitored throughout the product development life cycle. New information discovered during the development cycle must be used continually to question whether the project is sound. Further, all clinical trial outcomes need to be transparent among all collaborators. The impending failure of a sutureless anastomosis system by Converge Medical (Sunnyvale, CA), for example, might have been caught earlier and at lower cost if data had been shared openly among all stakeholders.[5] Instead, in 2005, the company failed its key clinical trial and was liquidated.

Regulatory issues contribute to technical risk. An estimated 30% of new products under development are combination products, most involving medical devices paired with pharmaceutical or biological components in some fashion.[6] For many manufacturers, however, such exciting combinations of biologics, drugs, and medical devices can raise a host of regulatory challenges. Similarly, venture capitalists funding such innovative approaches view regulatory issues as a major obstacle to product development and commercialization.

Combination product manufacturers face a major challenge in determining which FDA center will handle the application for market clearance. Ultimately, the responsibility for reviewing a combination product is assigned by FDA's Office of Combination Products. That determination is an important one, since there are substantial procedural and turnaround differences among the agency's three major centers, the Center for Biologics Evaluation and Research (CBER), the Center for Drug Evaluation and Research (CDER), and the Center for Devices and Radiological Health (CDRH).

The time it takes to turn around an application costs money, a particular concern to venture capitalists. Compounding the potential for long review delays, the Office of Combination Products saw a 42% increase in combination product review submissions from FY06 to FY07, the latest year for which figures are available (see Figure 1).[7]

(click to enlarge) Figure 1. Combination product submissions to FDA centers, FY03–07. The number of cominbation products submitted for review increased by 42% between FY06 (235) and FY07 (333), reaching a five-year high. All three FDA centers received increased applications for the review of combination products. Graph for FY03 represents data collection

The differences in regulatory pathways for each component of a convergent device can tremendously affect the phases in its life cycle, including preclinical testing, clinical investigation, marketing application, manufacturing and quality control, adverse-event reporting, promotion and advertising, and postapproval modifications. Significantly, combination products increasingly leverage state-of-the-art, innovative technologies that challenge existing regulatory and scientific knowledge, further slowing the FDA approval process.

Due Diligence and IP

Before entering into a collaborative relationship, there is no substitute for conducting thorough due diligence about all prospective partners. Examining their financial standing and business ethics are rudimentary first steps.

If a partner is bringing a key technology to the collaboration, it should be determined whether that partner has adequate freedom to operate for that technology and adequate intellectual property (IP) protection to defend its contribution. Issues

relating to the ownership of intellectual properties should be resolved in advance or during the early stages of product development, and protection of all variations and components of such products and technologies should also be accounted for.

beginning April 1, 2003. Source: FDA.

It is also important that the final partnering agreement define ownership of any joint IP the team develops. The partnership's legal structure should be tight enough to bind the required assets and resources together, but still sufficiently loose to allow all partners freedom to operate.

It is critically important that companies complete their due diligence before entering into a partnership. In addition to having an external market audit performed, companies should be aware of the ramifications of IP or clinical study results and how those may affect the ultimate success of a partnership.

Partnerships and Collaborative Relationships

Collaborative relationships can take many forms, and it is important at the beginning of a relationship to determine the chain of command and what protocol will be followed for communication.

At the beginning of any partnership, it is critical to get the right people involved. By involving people from across disciplines—taking into account the people actually doing the work, the cultural values of all the partner companies, who will be responsible for particular duties, and the communication protocol to be followed—everyone will understand what is to be accomplished (see sidebar).

In most life sciences partnerships, the collaborating companies are equally invested and act only on their own behalf. But many life sciences companies also outsource portions of their operations—from research and development through logistics and distribution. In many outsourcing arrangements, work is contracted out to a separate company, and it is often performed at sites outside the United States.

Many medtech companies also outsource by developing separate venture branches devoted to funding start-up companies.

The pervasiveness and variety of such arrangements suggest a need to review all contractual agreements with outsourcing firms and venture-backed firms when developing a partnering agreement. Each of the partners should ensure that such arrangements can be accommodated within the scope of the partnering agreement.

Emerging Technologies

Despite the challenges and hurdles, there are so many potential applications for innovative, convergent technologies that such an undertaking could be enormously profitable for companies and venture capitalists alike. With the financial success of drug-eluting stents, both life sciences companies and venture capital firms are now more willing to invest in combination products.

Lucrative market opportunities are emerging in the fields of nanomedicine, regenerative medicine, tissue engineering, neurotechnology, drug delivery, and spinal fusion (see Table I).

Technology or Segment	Market Size (est.), Current Status	Growth and Projection
Nanotechnology and nanomedicine	$12.4 billion invested by venture capitalists in 2006	17% annual growth rate; $110 billion by 2016
Orthobiologics	$2 billion	13% growth rate
Regenerative medicine	$5 billion	$10 billion by 2013
Spinal Fusion	$1.8 billion spent on spinal fusion devices	10.4% compound annual growth rate; $43.2 billion by 2012

Table I. Current status and projected value of healthcare market segments likely to benefit from convergence of technologies. Sources: Freedonia Group, Medtech Insight, Visiongain.

In the near future, regenerative medicine is expected to revolutionize the healthcare industry. Using biological approaches and biomimicry, regenerative medicine can help to restore, heal, and even regrow organs missing or damaged as a result of trauma or major diseases such as cardiovascular disease, Parkinson's disease, osteoarthritis, and dermatological disorders.

Similarly, in the spinal fusion market, more than $1.8 billion was spent on spinal fixation in 2006.[8] Combination products that mimic the cartilaginous and fibrous portions of the spine are now being explored and may soon replace spinal fusion.

Conclusion

Technological convergence has been very successful in a few commercialized products such as drug-eluting stents. But many other convergent technologies still remain in embryonic phases and have not entered the maturity curve. A careful review and examination of market trends and new opportunities in the healthcare industry, however, shows that the next generation of medical solutions will rely heavily on cross-sector collaborations devoted to exploring convergent technologies.

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