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such as toxicology and certain types of manufacturing. There is a continual need to manage the outsource partner, particularly to ensure that your project gets the priority it deserves. And it is a myth to think that it is inexpensive to outsource. The 'virtual' drug development model is not for every project; for example, it would not work in an environment where a lot of the expertise resides in a small number of talented

scientists, or where the technologies being applied to the development of a drug are novel and proprietary. However, the flexibility that is offered by an outsourcing model and the ability to exploit skills and resources, which would never be available in house without massive investment in infrastructure and equipment, makes the outsourcing model very sensible for companies involved in the late stages of pharmaceutical

development. I believe that the translation of early-stage research into clinical development and then marketable products is the area in which this model works best, and this is where AmpliMed is focused.

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Innovation drives success in Switzerland's biotech scene

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Today, it is not only Boris Becker and Ralf Schumacher who are choosing to set up home in Switzerland. A steady stream of profitable healthcare companies is selecting this country in central Europe as headquarters for healthcare-related research, development and production (Table 1). Attracted by favorable tax rulings and progressive business incentives, these companies also have access to Switzerland's highly skilled, educated and multilingual workforce. The latest to add their names to a growing list of companies with a presence in Switzerland are Celgene (new production center in the Canton of Neuchâtel) and Biogen Idec (European headquarters in Zug).

Strengths in pharmaceuticals

For years, Switzerland has been the home of innovative approaches to healthcare, built on its strong presence in the pharmaceutical industry. To a large part, this is a result of the success stories of Novartis and Roche, each with headquarters in the Basel area and each pursuing contrasting but successful business strategies in their global markets. Serono, Europe's largest biotech company, has its international headquarters in Geneva. On the strength of its portfolio in recombinant proteins, the company achieved worldwide revenues of US\$2.5 billion in 2004, a performance comparable to some of the leading biotech companies worldwide. Although successful healthcare companies can be found in many

regions of Switzerland, it is fair to say that the majority of early- and late-stage companies are located in the vicinity of three life-science clusters around Basel (40 companies, 4000 employees), Zürich (65 companies, 2000 employees) and the Lake Geneva region (30 companies, 5500 employees) (see map) [1]. This includes a dynamic medical technology sector, with enterprises like Medtronic (European headquarters in Tolochenaz), Phonak and Straumann.

Biotech future

A growing number of experts and opinion leaders are placing emphasis on biotechnology as the engine of growth for the healthcare industry in the years ahead. This emphasis is based on some clear-cut indicators. Last year, 26% of new active substances launched by the global pharmaceutical industry were biotech products (IMS LifeCycle New Products Focus). The Tufts Center for the Study of Drug

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TABLE 1

Some of Switzerland's life-science companies

Company	Expertise	URL
AC Immune	CNS disorders and cancer	www.acimmune.com
Actelion	Small molecule drugs	www.actelion.com
Addex Pharmaceuticals	CNS disorders	www.addexpharma.com
Arpida	Anti-infectives	www.arpida.ch
Basilea	Anti-infectives and dermatology	www.basilea.com
Berna Biotech	Vaccines and immunotherapy	www.bernabiotech.com
Card Guard	Wireless medical technologies	www.cardguard.com
Cytos Biotechnology	Immunodrugs	www.cytos.com
ESBATEch	Drug discovery	www.esbatech.com
The Genetics Company	Neurodegenerative diseases and cancer	www.the-genetics.com
Glycart Biotechnology	Therapeutic antibodies	www.glycart.com
Medtronic	Medical technologies including pacemakers, neurostimulators and other devices	www.medtronic.com
Phonak	Medical technologies to assist hearing	www.phonak.ch
Prionics	Prion diseases	www.prionics.ch
Speedel	Cardiovascular and metabolic diseases	www.speedel.com
Straumann	Implant dentistry and dental tissue regeneration	www.straumann.com
Symetis	Cardiovascular tissue engineering	www.symetis.com
Ypsomed	Self-injection devices	www.ypsomed.com

Development recently reported that of ~250 protein-based therapeutics currently in clinical trials, 33 recombinant-protein and 16 monoclonal-antibody therapeutics are likely to receive market approval from the FDA in the near future (press release available at <http://csdd.tufts.edu/NewsEvents/RecentNews.asp?newsid=52>). This is promising, considering that many of the protein therapeutics generated in the past 25 years of biotechnological endeavor (e.g. erythropoietin, interferons) have gone on to be blockbusters (revenues in excess of US\$1 billion). For countries willing to pursue technology development and the associated risks, opportunities clearly exist in global markets.

Rising stars in early-stage biotechnology

Across Switzerland, it is possible to see new biotechnology, medical-device and other life-science companies taking early steps on the road to profitability. This promise is reflected in successful financing rounds supported by international syndicates of investors as well as progress in development programs.

In Geneva, Addex Pharmaceuticals has proprietary compounds in pre clinical and

clinical development for the treatment of major central nervous system (CNS) indications, such as Alzheimer's disease, schizophrenia, anxiety, depression, pain and nicotine dependence. The company was recently selected by the US publication *Tornado Insider* as one of the Top 100 start-ups in Europe and Israel. Only last year, Addex completed the largest ever European Series B fund raising of €33 million, reflecting the confidence placed in it by investors and the scientific community alike.

In nearby Lausanne, AC Immune is adopting a novel immunological approach to the development of active and passive immune therapies for CNS diseases as well as cancer. Led by Andrea Pfeifer, the former head of Nestlé's Global Research in Vevey, Switzerland, AC Immune recently completed a private financing round of CHF21 million. The company's antigen technology platform is being used to generate conformational-sensitive antibodies suitable for active and passive immune therapies. The approach involves shifting the shape of key proteins, like β amyloid proteins implicated in the



FIGURE 1

The Zürich Biotech Center.

progression of Alzheimer's disease, away from a disease-causing conformation to a more stable, non-pathological structure.

Zürich, too, has a large group of early-stage companies looking to transfer innovative ideas to successful, sustainable and commercial undertakings. Symetis, a company founded in 2002 as a spin-off from the University of Zürich, is a privately held biotech company developing innovative, tissue-engineered heart valves for the replacement of badly formed or poorly functioning heart valves. Using a proprietary tissue-engineering approach, a living heart valve can be produced from patient's own vascular cells in a very short time [2]. The recently established Zürich Biotech Center (Figure 1), which is situated in Schlieren, is host to a promising array of biotech companies at different stages of development, including The Genetics Company (functional genomics), Prionics (neurological diseases), Glycart Biotechnology (therapeutic antibodies), ESBATEch (drug discovery) and Cytos Biotechnology (Immunodrugs™).

Track record for successful development

The new generation of early-stage companies in Switzerland has some successful, local role models to follow as it strives to bring much-needed therapeutics to the market. Several start-up companies have successfully negotiated the path from early-stage companies to publicly listed enterprises with global sales and market capitalizations to match. Actelion, with headquarters in Allschwil, is a recent example. This 2004 winner of the Biotechnology Industry Association's James D. Watson Helix Award discovers, develops and markets a range of drugs for the treatment of cardiovascular disease and other medical

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FIGURE 2
Medtronic European headquarters in Tolochenaz.

needs. Actelion, which recorded its first profit in 2003, is a good example of a successful spin-off from Roche, one of Switzerland's large pharma companies.

Serono is the long-standing role model of a successful, publicly listed biotech enterprise at home in Switzerland's climate for high-technology industries. By pursuing markets outside the interests of many larger pharmaceutical concerns, Serono has been successful by focusing on specialized markets, for example in neurology (Rebif), reproductive health (e.g. Gonal F) and growth and metabolism (e.g. Serostim). These success stories as well as 'success stories in progress' mean that Switzerland has made considerable progress in its efforts to foster innovation and entrepreneurship in the life sciences.

Strengths in academic research

It is often overlooked that universities drove the early days of the biotech industry and that they continue to be the source of innovative ideas for today's early-stage life-science companies. Genentech, a company with US\$3.7 billion in product revenues in 2004 and a market capitalization in excess of many of the pharmaceutical giants, was founded in the USA by a university scientist, Herbert W. Boyer, in cooperation with a venture capitalist, Robert A. Swanson. This successful formula of combining venture capital and scientific expertise continues to be followed by many life-science businesses. In 1980, when the biotech industry was just getting started, Biogen came into operations in Geneva, Switzerland, and was

founded primarily by academic scientists including Charles Weissmann (University of Zurich) and Nobel laureates Walter Gilbert and Phil Sharp from the USA. Today, Biogen Idec is one of the leading global biotech companies, serving patients in more than 90 countries.

In Switzerland, the presence of internationally renowned academic research institutions, primarily in the Basel, Geneva, Lausanne and Zürich regions, has enabled the transfer of innovation from the academic to the private sector. The Swiss Federal Institute of Technology in Zürich and Lausanne as well as world class universities in Geneva, Lausanne and beyond have an enviable record in education and

research. In addition, the Swiss Institute for Experimental Cancer and the Ludwig Institute for Cancer Research, based in the Lausanne area, have for many years pursued internationally recognized programs in oncology research. Swiss universities have also been successful in attracting talents back to Europe, as witnessed by the recent arrival of Ruedi Aebersold at the Swiss Federal Institute of Technology in Zürich, to help guide the development of a bold country-wide effort in systems-biology research.

A leader in bioinformatics

As the country that gave birth to the World Wide Web through research performed at CERN (Conseil Européen pour la Recherche Nucléaire) near Geneva, it is no surprise that Switzerland is pursuing far-reaching programs in informatics research. Geneva, Basel and Lausanne are home to research groups that are part of the Swiss Institute of Bioinformatics (SIB). Established in 1998, the SIB is an academic non-profit foundation promoting research, the development of databanks, such as the widely used SwissProt database of annotated protein sequences, and computer technologies related to the application of bioinformatics to the biological sciences. A recent multipartner, collaborative undertaking, the Vital IT project, is a large-scale computational research enterprise designed to support computer-intensive research applications in the life sciences.



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BOX 1

Some science parks and incubators in Switzerland

BioArk, Monthey

www.bioark.ch

Biopôle, Lausanne

www.biopole.ch

Eclosion, Geneva

www.eclosion.com

Fongit, Geneva,

www.fongit.ch

Fri Up, Fribourg

www.friup.ch

Neode, Neuchâtel

www.neode.ch

PSE Parc Scientifique, Lausanne

www.parc-scientifique.ch

Y-Parc SA, Yverdon-les-Bains

www.y-parc.ch

BOX 2

Some of Switzerland's technology transfer offices

- University of Geneva Technology Transfer Office (Unitec)
- University of Lausanne and the University of Lausanne Hospital Technology Transfer Office (PACTT)
- Swiss Federal Institute of Technology, Lausanne, Technology Transfer Office (SRI Industrial Relations Office)

Wealth for health

Switzerland has long been recognized as a long-term player in the global financial community. According to some estimates, Switzerland manages some US\$3000 billion in assets worldwide (http://www.pictet.com/en/home/about/history/gva_centre.html). Because investment is an essential prerequisite for any aspiring biotech company, access to financial assets, including venture capital, is a key ingredient for success. In the past few years, many countries in Europe have experienced a strong contraction in the amount of funding available for early-stage investments in what is often perceived as a high-risk industry. Switzerland, with its long tradition of financing life-science companies, has remained firm in supporting companies through venture capital. Between 2002 and 2004, Switzerland was ranked third by Ernst and Young among

European countries in terms of venture capital influx (CHF132, 125 and 194 million in 2002, 2003 and 2004, respectively). The presence of large biotech funds managed by banks, such as Clariden and Lombard Odier Darier Hentsch, as well as experienced European venture capital funds, for example Global Life Science Ventures, means that early-stage companies can benefit from the expertise and networks that these funds offer.

Medical technology presence

In addition to biotech prowess, Switzerland has strength in medical technology companies making products to improve or prolong the lives of patients. Since 1997, Medtronic has invested more than US\$80 million to build a state-of-the-art facility in Tolochenaz, overlooking Lake Geneva, serving its European, Middle East, African and Indian markets (Figure 2). It encompasses the world's most highly automated plants for the production of pacemakers and neurostimulators as well as a cutting-edge Therapy and Procedure Training Center, serving physicians and healthcare professionals from all over these regions. In 2004, Ypsomed, a medical technology company based in Burgdorf, which is developing self-injection devices allowing patients to administer their own medications in a safe and reliable manner, went public on the SWX Swiss Exchange. It has enjoyed a >90% increase in its share price since listing.

One of Europe's strongest healthcare stock exchanges

When it comes to the number of publicly listed life-science companies, the SWX Swiss Exchange is currently, after the London Stock Exchange (LSE), the leading European exchange in terms of public equity. Around one-third of its total market capitalization (33.8% as of April 2005) is due to companies active in the healthcare sector, which just exceeds the LSE (data as of May 2005, World Federation of Exchanges). These numbers testify to the strong pull of the SWX Swiss Exchange stock market as an attractive venue for the public listing of healthcare companies, both Swiss and international.

A credible future

Switzerland's success in the biotech sector has been founded on a sophisticated

scientific environment, highly skilled workforce as well as a supportive location for young innovative companies. Good relations with the European Union, a central geographic location and access to financial assets provide Swiss-based companies with an excellent means of accessing European markets for biotech products. The increase in revenues of Swiss-based biotech companies to CHF5.47 billion by the end of 2004 testifies to the ability of the country's biotech industry (CHF5.03 billion in 2003, 4.3 billion in 2002) [1]. Compared with the size of its population (~7.4 million), Switzerland has one of the highest densities of biotech companies worldwide. By the end of 2004, 133 core biotech companies were active in Switzerland [1] (Box 1 and 2).

Switzerland is taking further steps in its efforts to become a leader in the healthcare sector. For this purpose, it is investing further in infrastructure, including incubators and science parks that offer the right environment to nurture tomorrow's success stories. Innovative public-private financing schemes, such as those supporting the life-science incubator Eclosion in Geneva, are being encouraged. Organizations like BioAlps, a biocluster in the Lake Geneva region, are also helping to foster Switzerland's strength in the biotechnology and medical technology industries. Clusters serve to unite academic and private sector partners and also permit the sharing of resources and expertise. In turn, resources of this type can be used as part of a country-wide mechanism to encourage the formation and growth of early-stage companies. In the years ahead, Switzerland is poised for further success that will combine strengths in integrated, multidisciplinary biology with the commercial acumen needed to catalyze advances in the healthcare sector.

References

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