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ddt@elsevier.com

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Rapid growth in Israel's life science industry

Therese Barki, therese@idancom.com

In November 2004, two Israeli scientists from the Rappaport Research Institute and the Faculty of Medicine at the Israel Institute of Technology, Haifa, were awarded the Nobel Prize in Chemistry. Aaron Ciechanover and Avram Hershko, together with Irwin Rose from the University of California, Irvine, received the prize for their pioneering research and discovery of the ubiquitin system for protein degradation. This discovery has advanced our understanding of cellular processes, such as cell division and DNA repair, which are controlled by ubiquitin-mediated protein degradation. Ultimately, this knowledge might lead to the development of treatments for cancer and neurodegenerative disorders. The Israeli life science industry was obviously very pleased with the announcement.

Israel, with a population of 7 million, has the largest per capita number of scientists in the world, devotes 35% of its research grants to life sciences and is currently ranked third place in the world with regard to the number of new life science patents registered (www.uspto.gov and www.ilsi.org.il). According to Eli Opper, Chief Scientist of the Ministry of Industry, Trade and Labor (OCS), 'there are currently ten Israeli drugs in advanced stages of development (Phase I and II), positioning Israel as third in Europe in pharmaceutical development'. Opper is probably one of the most important people in the Israeli biotech industry today. He has given special attention to biotechnology, which is a rapidly growing area, and his top priority is to assist biotech companies. One way of helping is to promote biotech projects to get OCS grants. The OCS budget given to life science is growing steadily and over NIS300 million (over 25%) will have gone to this sector by the end of the year 2005. Another way of supporting biotech companies is to increase cooperation between academia and industry, technological incubators, start-up ventures, industrial R&D support and international cooperation, such as technology transfers, strategic alliances, workshops and seminars. Another exceptional aspect of support is the OCS's special biotechnology initiative to create a dedicated biotechnology accelerator, specifically designed to advance the development of high-potential early-stage drug candidates. This innovative program differs from the previous incubators sponsored by the OCS, as it allows for longer timelines and higher budgets required to advance drug development programs. The biotechnology initiative grant was awarded at the end of 2004 to BioLineRx and the BioLine Innovations Jerusalem (BIJ) accelerator opened its doors in January of 2005.

Ingredients to success

According to Aharon Schwartz, Vice President of Strategic Business Planning and New Ventures at Teva Pharmaceutical Industries, Israel's strength in the industry comprises three ingredients: 'an enormous concentration of scientific, specifically biological and medical, know-how. We have a culture of entrepreneurship, which enables us to get new ideas off the ground, and we are especially strong in developing medical devices' (Figure 1). Israel's strength in medical devices stems from its strong interdisciplinary capabilities and in particular the crossbreeding of biology and electronics. Israel is unique in the world in the sense that different sectors, such as defense, academia, medical and finance professions

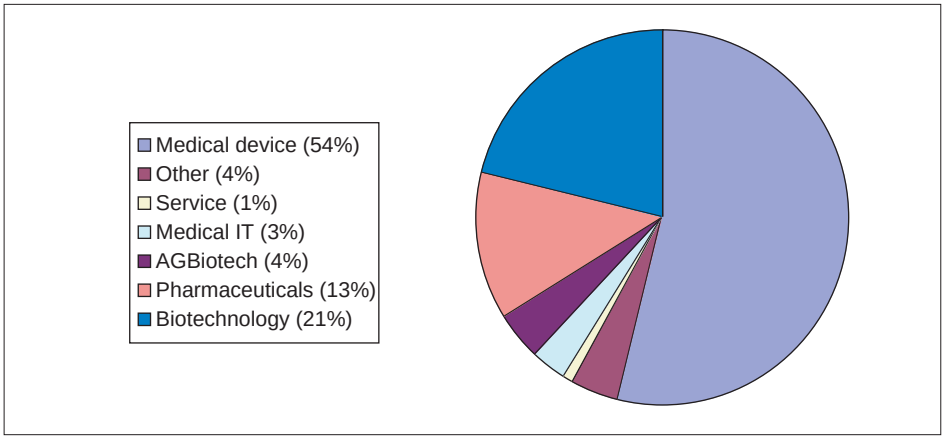

FIGURE 1

Sectors of Israel's life science industry. Figure modified, with permission, from ILSI: www.ilsi.org.il.

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biotech focus

and investors, all speak to each other. 'In recent years, Israel's medical device sector is attracting increasing amounts of foreign investment,' emphasizes Ruti Alon, General Partner at Pitango Venture Capital and Managing Director of HealthCare. 'This is achieved through venture capital funds, initial public offerings (IPO) and direct investments from major US and international companies like Johnson and Johnson, Boston Scientific, Medtronic and Guidant.' Israel has become one of the world's leading countries for the development of innovative medical devices and has in this sector the highest proportion of new patents per head of the population respect to any other country (www.ilsi.org.il). Another strength that makes Israel so unique is the TTCs (Technology Transfer Companies). Israeli universities have set up fully owned TTCs as separate entities to transfer pioneering research into applied ideas and marketable products. 'This is in contrast with the USA, where such TTCs are part of the university', explains Raphael Hofstein, President and CEO of Hadasit Medical Research Services and Development, the technology transfer company of the Hadassah Medical Organization in Jerusalem. Hofstein also explains that the TTC first identifies ideas with potential and then protects the intellectual property behind these ideas by taking out a provisional patent application (disclosure document), which the entire world must respect for two years if the idea is eventually patented.

'The country has one obvious weakness and that is a relative lack of capital', says Schwartz. 'If a professor at Massachusetts Institute of Technology or CalTech has a viable idea, raising money is not a problem. In the USA there is always money for good ideas, but in Israel, raising money is a constant struggle.' Zeev Weiss, Head of Strategic Planning of Life Science at PriceWaterHouseCoopers (PwC) explains that 'there is a variety of sources for financing in Israel. The funds derive from local and foreign venture capitals; collaborations with big pharmaceutical companies, based on outsourcing or selling parts of the company to finance the other projects; incubators that create a solution to pass the first stage of proof of concept (PoC); finance from multinational venture capitals, such as DARPA (Defense Advanced Research Projects Agency), NIH (National Institutes of Health), and finally, from private investors that already made an exit and are looking for new opportunities.'

Bridging the gap between innovation and the industry

An interesting example of ways to bridge between great innovations in early stages and the industry is BioLineRx, which was established in 2003 by Teva, Giza Venture Capital, Pitango Venture Capital, the Jerusalem Development Authority and Hadasit. BioLineRx is Israel's leading specialized drug development company, and its BIJ subsidiary is the first biotech-dedicated incubator in Israel. BioLineRx's mission is to build a robust pipeline of proprietary therapeutic products for unmet medical needs. The company is focused on evaluating, acquiring and advancing projects from lead selection to advanced clinical trials, regulatory approval and marketing. BioLineRx was founded with an initial investment of US$23 million, which is supplemented by the US$21 million BIJ grant, and is structured to in-license promising compounds and accelerate their development into the clinic and beyond. Projects under development include treatment of fatty liver disease, a scaffold to reduce cardiac damage after heart attack and innovative preclinical molecules for the treatment of cancer and inflammatory bowel disease. BioLineRx recently announced that its lead project, BL-1020, for the treatment of schizophrenia, will be entering human clinical trials in the first quarter of 2006. Morris Laster, CEO of BioLineRx, states that 'the original approach represented by BioLineRx might be the wave of the future in how to successfully develop early stage compounds and provide effective translation of basic R&D to clinically viable compounds.' The fact that the OCS recognized the possibility of functioning as a project incubator enables BioLineRx to bring together the personnel necessary to perform professional drug development. In addition to BioLineRx in Jerusalem, over 20 technology incubators in Israel are spread out all over the country, from Kiryat Shemona in the north to Sde Boker in the south. Since 2003, 12 of the existing incubators have been privatized and transformed into 'for-profit' companies. Privatizing incubators is, on the one hand, OCS's way of enhancing the involvement of private investors and making their responsibilities heavier and, on the other hand, giving them the opportunity to benefit from a project's success.

Advancing the life science industry

To help advance the life science industry, Alon set up the nonprofitable organization ILSI (Israel Life Science Industry) together with Israeli life science colleagues Yossi Bornstein, CEO of Shizim, Raphael Hofstein, CEO and President of Hadasit, and Zeev Zelig, Vice President and General Manager of Genzyme ITG. ILSI was established to act as an umbrella organization covering the various components of Israel's life science community, which includes pharmaceuticals, biotechnology, medical devices, agricultural biotech and related services. With 550 companies (www.uspto.gov and www.ilsi.org.il), the life science cluster is comparable in size with the major US life science clusters in Silicon Valley, San Diego, Minneapolis and Boston. ILSI provides

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BOX 1

Rapid Growth in the Israeli life science industry:

Copaxone, developed at the Weizmann Institute, Rehovot, by Michael Sela and Ruth Arnon, treats multiple sclerosis and is the first pharmaceutical that has been developed in Israel from the laboratory through to market launch. In 2004, Copaxone brought Teva sales of US$900 million and is estimated to break the billion dollar barrier this year (Table 1).

Exelon, developed by Marta Rosen Weinstock of the Hebrew University, Jerusalem, treats Alzheimer's disease and was sold to Novartis using a technology transfer agreement that earns Novartis hundreds of millions US$ a year in sales (Table 1).

Doxil (doxorubicin HCl liposome injection), developed by Yechezkel Barenholtz of the Hebrew University, Jerusalem, is an infusion treatment for cancer (ovarian, Kaposi sarcoma) and was sold to Johnson and Johnson using a technology transfer agreement that earns Johnson and Johnson hundreds of millions US$ a year in sales (Table 1).

TABLE 1

Worldwide known drugs developed in Israel[a]

Company	Drug	Indication	2004 sales (US$ millions)
Savient	Oxandrin	Anabolic drug	45
Johnson and Johnson	Doxil	Cancer (ovarian, Kaposi's sarcoma)	200[b]
Serono	Rebif	Multiple sclerosis	1090
Serono	Gonal-f	Infertility	570
Teva	Copaxon	Multiple sclerosis	1000
Novartis	Exelon	Alzheimer's disease	425
Total			**3.33 billions**

[a]Data from ILSI: www.ilsi.org.il

[b]Data relate to 2002 (data for 2004 not available)

Rasagaline/Azilect®, developed by Moussa B.H. Youdim of the Rappaport Institute Haifa, Technion and Teva, provides a treatment that significantly improves Parkinson disease's symptoms throughout the course of the disease. The drug is already approved and sold on the European market since 2004 and is expected to be approved by the FDA soon.

Predix Pharmaceuticals Holdings, based in Ramat Gan, Israel, formerly Israeli Bio Information Technologies, is a pharmaceutical company focused on the discovery and development of novel, highly selective, small-molecule drugs that target G-protein-coupled receptors (GPCRs) and ion channels. Using its proprietary drug discovery technology and approach, Predix has progressed three drug candidates into clinical trials and has six additional programs in preclinical development and discovery.

Given-Image, based in Yokneam, Israel, is Israel's best-known medical-device company. It has redefined the way gastrointestinal diagnosis is carried out and is recognized as the gold standard in detecting disease of the small intestine, resulting in more-accurate diagnosis of a range of gastrointestinal disorders. The company's flagship technology, the Given Diagnostic System, features the naturally ingested PillCam™ video capsule endoscopes, including the PillCam™ SB for the small bowel, which was approved by the FDA in 2001, and the PillCam EOS for the esophagus, which was approved in 2004.

BioLineRx, Jerusalem (www.biolinerx.com)
See article.

ProChon Biotech, Rehovot (www.prochon.com)
Established in 1997, ProChon Biotech's vision is to become a world leader in regenerative medicine by combining proprietary growth factors, scaffolds and state-of-the-art cell technologies with deep understanding of the target tissue biology. Biocart™II, is a second generation tissue-regeneration implant for the treatment of joint cartilage defects. It provides long-term repair of cartilage defects and halts the degenerative process, which usually leads to further cartilage degeneration and loss of joint function.

TransPharma Medical, Lod (www.transpharma-medical.com)
Established in 2005, TransPharma Medical is a biopharmaceutical company focused on the development and commercialization of pharmaceutical products utilizing its proprietary active transdermal drug delivery technology. This patented technology is employed in its drug delivery system ViaDerm. The ViaDerm system, designed for home use, enables painless, needle-free, user-friendly drug delivery through the skin.

CureTech, Yavne (www.curetech.co.il)
CureTech, established in 2001, is a biotechnology company focused on research, development and commercialization of innovative broad-spectrum immune modulating products for the treatment and control of cancer. The company's products are antibodies and peptide-based vaccines designed to enhance immune response, directing it against the developing cancer. At the beginning of 2005 CureTech's lead humanized antibody product, CT-011 already finished Phase I clinical testing, and is currently in Phase II with FDA negotiations.

the life science community a united voice, with which to communicate with public officials and investors in Israel and worldwide. To help spread information, ILSI built an internet site (www.ilsi.org.il) that makes sure information is available to political leaders, news media, venture capitals, investment bankers, and the public. It is the exact information required by potential investors, be it strategic corporate players or financial investors worldwide.

Despite the obstacles in raising funds, the year 2005 is characterized by an optimistic view on Israeli life science industry (Box 1). It is only a matter of the right combination of a 'technology-scientists-business' model and a convincing strategy for fund investors to come to the biotech industry in Israel.

Therese Barki
Director of International Marketing Communications,
Idan Corporate Image Communications,
P.O.B 168, Rishpon,
46915 Israel