

# **SRAEL HIGH-TECH & INVESTMENT REPORT**

A MONTHLY REPORT COVERING NEWS AND INVESTMENT OPPORTUNITIES  
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## **Biotechnology Points to a Tantalizing Future**

The Bio-Tech Israel 2003 week served as an outstanding showcase for developments in this field. More than a 130 companies participated and exhibited their products and technologies. Industry, government and academia leaders, presented an overview of Israeli biotech and their projection for future achievements.

In the absence of recent statistics, 140 is the generally accepted figure for the number of companies active in this field. The industry employs more than 4,000, and its output is in excess of \$800 million a year. The figures however, reflect a distortion in industry output statistics. Teva Pharmaceuticals alone, was responsible in 2002 for more than \$550 million in exports of its Multiple Sclerosis Copaxone drug.

The number of start-ups in the biotechnology industry is high and equals the number of companies in countries such as Switzerland, Sweden, and France. Were it not a field, where from the laboratory to the market place, is both a laborious and extremely lengthy process, the industry's output would be considerably greater. Nevertheless, the relatively large number of companies that are currently intensively busy in developing therapeutical pharmaceuticals, diagnostic and other biotechnology related products, are to be seen as a barometer for substantial future growth.

Israel's medical device industry, numbering more than 400 companies, is taking due notice of the possibilities opening up for combining medicinals with medical devices. Israel has traditionally been one of the global leaders in cardiac stents, with names like InStent and NIR well known. With the debut of

Johnson & Johnson Cypher medicated stent, accompanied by the belief that it will become a multi billion dollar product, there is impetus for developers to contemplate other type of "device/pharma" combinations.

Israeli researchers such as Professor Itskovich of Haifa's Rambam Hospital, speak of the prospects of "biological intervention as compared with medical intervention".

On August 9, 2001 the American debate on the use of stem cell lines began as

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President Bush announced his guidelines for making research funding available based on the existing 64 stem cell lines. Four of these are to be found in Israel and are being used by Prof. Itskovich and his group for scientific research purposes.

Since the isolation of human embryonic stem cells four years ago, excitement is being generated and prospects are being mentioned for the use of these cells to produce various types of tissues in our body. It is no longer a fantasy for the successful growing of precursors of heart cells from human embryonic stem cells.

It is the first time that human, as opposed to mouse stem cells have been induced to form proto-heart cells. In addition, human embryonic stem cells have been made to differentiate into heart cell tissue. Moreover, the techniques developed could produce other types of human tissue.

The next step in moving towards clinical applications, such as injecting these cells into damaged human hearts, is to significantly increase the number of cells produced.

Improved sensors, as presented by one company, will allow the minimally invasive surgeon to improve on his technique and results.

While Israel's biotechnology industry is not expected to develop exponentially yet the diversity of its research and development, leaves ample room for joint venture agreements with global companies, who would prefer the development to be done by others. Past history make the future seem very promising.

One only needs to be reminded that Novartis' anti-Alzheimer's drug Exelon, with sales in excess of \$320 million in 2002 was discovered by the Israeli researcher Prof. Martha Roisen of the Hebrew University of Jerusalem.

Equally impressive is the achievement of Prof. Yehezkel Barenholz, also of the Hebrew University who is responsible for the development of the liposomal delivery system which is the basis of Doxil, an improved anti-cancer drug. Johnson & Johnson had sales of \$210 million in 2002.

### ***Prof. A. Ciechanover Awarded Israel Prize***

Biologist Aharon Ciechanover of the Technion has this year been awarded the Israel Prize for biology for his research into the mechanisms that contribute to the stability of protein cells, which has ramifications for molecular research and for cancer studies.



### ***The Best of Biotech was on Display***

Two years ago, the Chief Scientist's Office commissioned the Monitor Report, an independent study of the potential of the local biotech industry. The report provided favorable forecasts with the authors recommending that the government invest \$105 million in biotechnology over a period of four years, in order to bring the local industry to a revenue turnover of \$2-3 billion by 2010.

However, the global business climate has deteriorated since then and in the first half of 2002, Israel saw a 50 percent drop in capital mobilization for its life sciences companies, as compared with a year earlier.

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Yet the Government sponsored Monitor report projected, that revenues of Israel biotechnology companies might reach 2-3% of total sales of the global biotechnological industry. which are projected to exceed \$40 billion by 2004 and \$100 billion by 2010.

According to that report, the industry's challenge is to help companies to become more established and "make available to the firms physical, regulatory and scientific infrastructure".

### ***The Cream of the Crop***



**Baby's Breath** showed an "active hood" that facilitates drug-inhalation treatment. The number of babies that suffer from breath related conditions such as asthma and bronchitis is increasing steadily with 20%-30% of Western babies in need of drug-inhalation treatments.

**Senesis** showed at Biotech 2003 a miniature automated device that allows

fast DNA and protein analysis. The handheld device is in advanced stages of development and is designed for a broad range of medical, research and food industry applications.

**Gavish-Galilee Bio Applications** unveiled a technology for growing Morchella mushrooms in controlled hothouse conditions. Similarly to truffles, the Morchella mushrooms are also rare, expensive and found only in specific regions around the globe.

The Morchella mushrooms, more popularly known as Morel, grow naturally in forests and in special climatic conditions along the equator at 40°. Most of the Morel mushrooms marketed around the world grow naturally in forests in Europe, the USA, Canada, India, Pakistan, Afghanistan, China, Turkey and Nepal. However, total exports from India, Pakistan, Nepal, and Turkey amounts to just 150 tons per annum, which pushes the mushrooms consumer price up to USD 400 for one kilo.

**Vascular Biogenics Ltd. (VBL)** exhibited an innovative development of a genetic treatment, designed to destroy the walls of the blood vessels that provide oxygen to carcinogenic metastases. The company says that the treatment is effective for a variety of cancer tumors and results in dramatic reversal of the tumor, with no toxic side effects. Designed for patients that suffer from metastatic cancer, the new treatment is administered by systemic injections in addition to chemotherapeutical or radiation treatments.

**Topimed**, a startup operating as part of Ashkelon, Israel, Technological Incubator, will show a unique medical preparation for treatment of skin damage. Designed for treating degenerative processes of the skin, and wrinkles that result from natural ageing and sun radiation, the new preparation acts both on the dermal and epidermal cells, thus healing the internal skin layers and resulting in improved appearance.

**Medvision** exhibited a novel system that monitors lesions that might indicate the development of melanoma skin cancer. The system is targeted for general practitioner clinics or for melanoma patients.

## Getting Under the Skin

### ***IHTIR is Introduced to a Novel Way to Deliver Drugs***

Transdermal drug patches offer the advantages of ease of use, painlessness, disposability, control of drug delivery and avoidance of first-pass metabolism by the liver. However, current transdermal patch designs are not capable of transporting large molecular drugs through the skin barrier, especially peptides and proteins, which include many drugs that are marketed, or will emerge, from the biotechnology industry. As a result, a variety of approaches are being investigated by companies for enhancing transdermal drug delivery. They include the use of iontophoresis, ultrasound (sonophore-

sis), electroporation, heat and microneedles. One product in the offing is for the delivery of nitroglycerine for angina pectoris.

TransPharma Medical Ltd. (Yehud, Israel) is headed by its founder Dr. Daphna Hefetz. It employs microscopic passageways for the controlled transdermal delivery of macromolecules. Radiofrequency energy is used to ablate the outer layer of skin, thereby creating microchannels of precise dimensions, called RFMicroChannels, that enable the controlled passage, of small and large molecules through the skin, via an applied adhesive patch. The initial product to be developed, ViaDerm, is a two-stage system consisting of a reusable handheld device, that incorporates a disposable microelectrode array that transmits RE energy, and a patch containing the drug that is applied after creating the microchannels. Its safety has been demonstrated in a human trial for single and repeat applications.



Though founded less than three years ago, TransPharma, early in its history, obtained patent protection. The company has completed safety trials, as well as first stage live animal trials. Reportedly, the company is in the stages of receiving United States Food and Drug Administration (FDA) approval to market its products in the U.S.

#### Two Rounds of Financing

In July 2001 TransPharma raised \$6.5 million from Biomedical Investments, Pitango Venture Capital and Discount Capital Markets and Investments. A second round followed in April 2003 when it secured \$8 million in venture funding in a round led by Evergreen.

Dr. Hefetz obtained her Ph.D in biochemistry from the Weizmann Institute in 1991 and continued to a post-doctoral fellowship in molecular biology. Prior to founding TransPharma, Dr. Hefetz headed Savyon Diagnostics.

"The company is 4-6 years away from the market", Dr. Hefetz told IHTIR. "The strategy is to cooperate with a big pharma so as to raise the valuation and to generate positive cash flow," she added.

## Science Corner

### *Greenhouse Gas Might Green up the Desert*

Missing: around 7 billion tons of carbon dioxide (CO<sub>2</sub>), the main greenhouse gas charged with global warming. Every year, industry releases about 22 billion tons of carbon dioxide into the atmosphere. And every year, when scientists measure the rise of carbon dioxide in the atmosphere, it doesn't add up - about half goes missing. Figuring in the amount that could be soaked up by oceans, some 7 billion tons still remain unaccounted for. Now a study conducted at the edge of Israel's Negev Desert has come up with what might be a piece of the puzzle. A group of scientists headed by Prof. Dan Yakir of the Weizmann Institute's Environmental Sciences and Energy Department found that the Yatir forest, planted at the edge of the Negev Desert 35 years ago, is expanding at an unexpected rate. The findings, published in the current issue of *Global Change Biology*, suggest that forests in other parts of the globe could also be expanding into arid lands, absorbing carbon dioxide in the process.

The Negev research station is the most arid site in a worldwide network (FluxNet) established by scientists to investigate carbon dioxide absorption by plants.

The Weizmann team found, to its surprise, that the Yatir forest is a substantial "sink" (CO<sub>2</sub>-absorbing site): its absorbing efficiency is similar to that of many of its counterparts in more fertile lands. These results were unexpected since forests in dry regions are considered to develop very slowly, if at all, and thus are not expected to soak up much carbon dioxide (the more rapidly the forest develops the more carbon dioxide it needs, since carbon dioxide drives the production of sugars). However, the Yakir forest is growing at a relatively quick pace, and is even expanding further into the desert.

Why would a forest grow so well on arid land, countering all expectations ("It wouldn't have even been planted there had scientists been consulted," says Professor Yakir) The answer, the team suggests, might be found in the way plants address one of their eternal dilemmas. Plants need carbon dioxide for photosynthesis, which leads to the production of

sugars. But to obtain it, they must open pores in their leaves and consequently lose large quantities of water by evaporation. The plant must decide which it needs more: water or carbon dioxide. Yakir suggests that the 30 percent increase of atmospheric carbon dioxide since the start of the industrial revolution eases the plant's dilemma. Under such conditions, the plant doesn't have to fully open the pores for carbon dioxide to seep in - a relatively small opening is sufficient. Consequently, less water escapes the plant's pores. This efficient water preservation technique keeps moisture in the ground, allowing forests to grow in areas that previously were too dry.

The scientists hope the study will help identify new arable lands and counter desertification trends in vulnerable regions.

The findings could provide insights into the "missing carbon dioxide" riddle, uncovering an unexpected type of sink. Deciphering the atmospheric carbon dioxide riddle is critical since the rise in the concentrations of this greenhouse gas, is suspected of driving global warming and its resulting climate changes.



Tracking down carbon dioxide sinks could help scientists, better assess how long such absorption might continue and lead to the development of efficient methods to take up carbon dioxide.

***Venture Capital Raising Falls to Nine-year Low***

Venture capital fund-raising in the United States in the first quarter of 2003 fell to \$996 million, its lowest level since the third quarter of 1994, according to data compiled by Thomson Venture Economics for the National Venture Capital Association.

This year's first-quarter represented a 41 percent decrease from the same time last year, when venture capitalists raised \$1.68 billion for future investments, the study said.

**Tough to Raise a Dollar**

Israeli life sciences companies raised only \$30 million in the first quarter of 2003, down 40% from fourth quarter of 2002, says Ernst & Young Israel biotech partner Yoram Wilamowski. No less than 25 life sciences firms collapsed last year, according to Wilamowski, while only six new life sciences ventures started up.

Veteran companies are mostly hurt by non-renewal of agreements with multinationals or from a lack of new agreements as they cut research and development budgets. The younger companies suffer from the multinationals substantially decreased interest in risky projects with far-term revenue projections.

***Zetiq Technologies is Entering a Hot Field of Biotech***

The tedious procedures of laboratory chemistry are being overshadowed by machines that combine the power of computers, lasers, optical reading systems and robotics.

The whole effort is expressed in a catchall phrase that is heard very often: "high throughput screening" (HTS). Hundreds or thousands of chemical targets are arrayed on a tray or slide and subjected to very rapid analysis. For example, if a researcher wished to test hundreds of patented drug molecules, looking for those that bind to a docking site on a protein, a machine of this sort would do the job in hours.

Each well of chemicals could be tagged with a fluorescent marker and the protein under study would be added to miniaturized test tubes of the experimental array. A reaction would give off light that can be easily read electromechanically and translated onto a computer data base.

The company has developed an ability to screen for a previously undetectable indication: of non-cytotoxic anti-cancer drugs. These drugs encompass most of the therapeutic mechanisms presently regarded as the future of anti-cancer therapy, such as oncogenic signal inhibition, malignancy reversions and differentiation therapy, while excluding the



conventional ineffective cytotoxic, cytostatic and apoptosis inducing drugs.

By implementing this highly innovative approach, ZetiQ has already generated an impressive number of hits against colon cancer. Dr. Dan Gelvan, ZetiQ's founder and CEO, is a supporter of joint venturing early in the career of young companies. He is currently negotiating just such a relationship with as yet an unidentified company.

### ***Bio-Tech: Looking Back and into the Future***

Dr. Yaffa Beck is a leader of Israel's biotech industry, and a co-founder of D-Pharm. She currently serves as CEO of VentuRx Holdings, and is quoted below from her conference opening remarks.

The Israeli industry has had some substantial achievements in 2002-2003:

**In manufacturing** - BTG inaugurated its new state of the art cGMP plant in Kiryat Mal'Achi.

**In sales** - InterPharm, celebrating its Silver jubilee, reported more than \$600M of Rebif for MS sales, by partner/owner Serono; Teva recorded sales >\$550M of Copaxone for MS.

**In clinical development:** Reported successes of D-Pharm, Peptor, XTL, Pharmos and others.

**In partnering:** Multi-million \$\$\$ agreements signed with international pharma by Peptor, ProChon, QBI, Compugen and others.

Several companies raised **follow-on investments**- Canfite, Procognia, Medgenics.

Israeli biotech is world-renowned for its scientific innovation and entrepreneurial spirit. The best, most exciting and most advanced of Israeli biotech technologies and products will be show-cased over the next three days of the conference in multiple technology sessions. As you will listen to the talks, you may note that there are some unique clusters of competitive advantages in Israeli biotech.

Stem Cell research

Neurological and neurodegenerative disease research.

Cancer research.

Drug-device combinations research.

I would like to call the attention of the private sector to the opportunities - this is your day.

Valuations - as we all know - are very low now

Cash is king!

Thus, I call on the biotech investors to get off the 'fence'- by big-time investing in the Israeli start-ups - which have the technologies and compounds ready for development - and which are starved for cash.

I also call on the Entrepreneurs - to listen to their experienced VC investors, focus their efforts, conserve their cash, and be mindful to the market's needs

This is the time to use our 'collective wits' and 'Jewish chutzpah' - as a community, as an industry, to find the ways and the means to challenge the odds that are currently stacked against us and forge a path for success.

### ***Remarks by the Chief Scientist***

Dr. Eli Opper, Chief Scientist, at the Ministry of Industry and Trade commented that: "Israeli biotechnology is particularly strong in biotherapeutics with three therapeutic areas leading: neurology disorders, cancer and autoimmune syndromes. These happen to be the fastest growing markets worldwide. About 50% of university research projects in therapeutics and 60% of biotech drugs in the pipeline are in the therapeutic areas. Israel has an exceptionally strong academic base in these disciplines and one of the largest reservoirs of science-skilled human resources, with 900 senior faculty members in biotech related departments. and a third of all PhD graduates coming from biotech related programs. Known for having the largest population of scientists per capita in the world, 35% of all research in Israel concentrates on life sciences".

### ***Milestones Reached in 2002***

Putting aside the unsettled economic conditions in the USA and Israel, 2002 was marked by a number of major achievements by Israel's biotech sector. BioTechnology General, one of the country's first biotech companies launched its brand new, state-of-the-art cGMP plants. InterPharm Laboratories continued its \$90 million production expansion program. Teva Pharmaceuticals was able to point to Copaxone sales of more than half a billion dollars. Copaxone is the first "blockbuster drug" developed and manufactured in Israel. The drug treats certain issues of Multiple Sclerosis.

Betting on the future of biotechnology in Israel Teva, together with venture capital funds Giza, Pitango, and Hadasit, the research and development arm of the Hadassah Medical Organization, established Bioline Therapeutics to promote the activities of early stage projects and companies.

While raising capital for biotechnology was a difficult endeavor nevertheless some companies attracted new funds. Among these were Can-Fite BioPharma whose lead drug candidate has moved through Phase I and is shortly expected to launch Phase II trials. The drug is aimed at treating colorectal cancer and for rheumatoid arthritis.

BrainGate has announced that it will apply the funds raised to develop medical equipment and begin clinical trials on the treatment it has designed to improve delivery of drugs for diseases such as brain tumors and neurological degenerative conditions.

ProCognia will apply funds raised towards its research and development program related to glycoprotein drugs.

Medgenics' newly raised funds are aimed at enhancing its protein delivery technology.

The major cooperative agreement of the year was forged by Peptor, which signed a licensing agreement with Aventis for its diabetes drug. Peptor is active in developing synthetic peptide-based pharmaceuticals. The company is also cooperating with Roche in developing cancer treatments.

QBI, a company that specializes in pathology specific drug delivery, signed a cooperation agreement with the Japanese Fujisawa company.

ProChon Biotech active in developing proprietary know-how in growth factors, entered into a strategic agreement with Morphosys.

### ***VisionCare's Implantable Miniature Telescope for Macular Degeneration***

Positive Phase I clinical trial results, were reported recently for the Implantable Miniature Telescope, a telephoto ocular prosthesis designed to improve impaired central vision in patients with macular degeneration, a disease of the central retina. The results, based on twelve-month clinical data, were presented in the Retinal Prosthesis session at the annual meeting of the Association for Research in Vision and Ophthalmology (ARVO) in Fort Lauderdale, Florida.

In the Phase I U.S. IMT-001 trial, sponsored by VisionCare Ophthalmic Technologies, Inc., the Implantable Miniature Telescope by Dr. Isaac Lipshitz was evaluated in patients with moderate to severe bilateral central vision impairment.

AMD is the leading cause of irreversible vision loss in individuals over the age of 50. The clinical data, presented by Dr. Hamill, included fourteen patients that were implanted with the IMT. Trial participants were 60 years of age or older, had bilateral atrophy or scarring AMD and visual acuity no better than 20/80, but no worse than 20/400.

"The preliminary safety and efficacy data from this trial are encouraging. We are pleased with the safety profile in this pilot study, including the preservation of critical ocular structures during and after implantation of the IMT. We are hopeful that both the safety performance and patient benefits seen in this study will be confirmed in the larger Phase II/III trial which is currently enrolling patients," said Dr. Hamill.

"These results are promising, and with further study, we may finally have a treatment option that can permanently improve vision in patients with stable, late-stage macular degeneration," commented Baruch D. Kuppermann, retina specialist at the University of California, Irvine, and an IMT-001 investigator. "The loss of central vision caused by this debilitating retinal disease can severely affect one's ability to perform everyday activities. Although not curative, these results offer hope of enhanced central vision for the large population afflicted with macular degeneration," he added.

The IMT is a proprietary multi-lens ocular prosthesis, about the size of a pea, which is implanted in one eye in an outpatient surgical procedure conducted under local anesthesia. The optical portion of the IMT is a precision telescope, incorporating micro-lenses, that provides magnification of 3.0X or 2.2X, depending on the IMT model used. A 3.0X IMT was utilized in the IMT-001 trial. This telephoto device renders a magnified image over a wide field of the retina to improve the ability to recognize images that were previously either difficult or impossible to see. The IMT is implanted in one eye, which provides central vision, while the non-implanted eye provides peripheral vision.

About Macular Degeneration and Stargardt's Disease

Macular degeneration is a disorder of the retina, the thin light-sensing layer lining the back of the eye. The condition affects the central retina, or macula, which is responsible for detailed vision that controls important functional visual activities like reading, recognizing faces, and watching television

About VisionCare  
VisionCare Ophthalmic Technologies, Inc., is a private, venture capital funded company involved in the research, development, manufacturing, and marketing of innovative and proprietary ocular prosthetic devices for the treatment of macular degeneration and other vision disorders.

VisionCare is headquartered in Saratoga, CA and has research facilities in Yehud, Israel. The IMT was invented by Israeli scientists Dr. Isaac Lipshitz and Yossi Gross.

### ***Financing: Hard to Find and Expensive***

We left Bio-Tech 2003 with the impression that at least in 2003 and perhaps well into 2004, the sector will be facing a repeat of the difficult days in the 1990's, when capital was both hard to find and very expensive.

Biotechnology unlike other high-tech industries that are human resource intensive, is also highly capital intensive. The initial cost of product development is only a fraction of the overall cost. Creating a new pharmaceutical, for one example, is an awesome task, which requires hundreds of millions of dollars. The emerging developing companies on exhibit, for the very greater part have adopted a "joint venture partner" orientation. They are keenly aware that they can serve as "first rate research and development bucket shops" but can not muster the funds required to get to the starting point to the market place.

Nevertheless, we expect that more than a few of these companies, some of which we have featured or mentioned in passing, will provide a needed product or service that will lead to commercial success as well as provide a return to the investors that have shown their faith.

Vascular Biogenics Ltd., the company that has developed a genetic treatment designed to destroy the walls of the blood vessels that provide oxygen to carcinogenic metastases says that the treatment is effective

for a variety of cancer tumors and results in dramatic reversal of the tumor with no toxic side effects. Prof. Dror Harats. VBL's CEO sounded upbeat. He is currently in negotiations for an joint eventure with a medical firm that will provide the support to move his company to the next state of development.

### ***Prof. Michael Sela: Needed More Budgeting for Science***

"As humanity heads into the third millennium, the greatest impact - but also the greatest challenge - is the ever increasing amount of information and communication, particularly in the natural sciences. The progress here is truly enormous and it is sometimes running ahead of its legal, ethical and moral aspects. But as with all progress we must avoid an excess of information becoming a barrier to comprehension. In parallel, we must ensure that the work being done in research ultimately benefits humankind and human civilization. For countries that invest in research and the development of new technologies, it is important to translate the accumulated knowledge into benefits for their population in order to justify those investments to the taxpayer.

Inventing, developing, and marketing a pharmaceutical is an activity that suits Israel. However, the major restraint is probably the inadequate budgeting for scientific research and development on the country's campuses.

Research and development is carried out primarily at the universities. As everywhere, the advancement of basic scientific knowledge is the chief objective of researchers at Israel's universities. In addition to their scientific research activities, the universities continue to play an important role in the country's technological advancement".

About 100,000 students are enrolled in Israel's universities, with about 18 percent of all undergraduate students and 50 percent of all Ph.D. candidates specializing in the sciences or medicine. Another 13 percent of all undergraduate students and 10 percent of all graduate students specialize in engineering and architecture. Relative to the size of its labor force, Israel has a significantly larger number of publishing authors in the natural sciences, engineering, agriculture and medicine than any other country. Statistics also show that Israel has a



larger share of publications co-authored by Israeli and foreign scientists than any other country, indicating international scientific co-operation.

Altogether, Israel spends \$260 million annually on academic research, most of the money coming from the government and administered by the Council for Higher Education's Planning and Budgeting Committee. In addition, research authorities within the universities help faculty members locate, apply for and administer external research grants. There are at least 300 such sources, including ten large foundations, most of which involve foreign donors and require collaboration with foreign scientists. All in all, grant programs support about 2,000 research projects at an annual cost of \$70 million. Israeli researchers also successfully compete for foreign grants and fellowships.

A recent study shows that the universities are Israel's leading patentees at home and abroad, and that the relative size of their patenting activity far exceeds that of higher education sectors in other countries.

A doubling of the allocation to \$520 million, would bring the outlay to \$5,200 per student but the results would be much significant and far-reaching.

***Copaxone: Born Locally, "Made in Israel" and Sold to the World***

In September 1996 - An advisory committee convened by the U.S. Food and Drug Administration recommended that the FDA approve the Israeli drug copolymer-1, to be marketed under the brand name COPAXONE®, for treatment of patients with relapsing-remitting multiple sclerosis.

Following the recommendation, the FDA granted approval for the marketing of the drug in the U.S. Copolymer-1 (COPAXONE®) is a protein-like molecule originally synthesized and developed by Prof. Michael Sela, Prof. Ruth Arnon and Dr. Dvora Teitelbaum of the Weizmann Institute of Science in Rehovot, Israel.

Yeda Research & Development Co., which deals with the commercialization of Weizmann Institute research, granted exclusive rights for manufacturing and for marketing copolymer-1 (COPAXONE®) throughout

the world to Teva Pharmaceutical Industries Ltd., Israel.

The drug was developed by Teva, with the participation of physicians and researchers from Israel and other countries. Clinical trials have shown that copolymer-1 reduces the number of attacks in patients with the relapsing-remitting form of multiple sclerosis, and that it improves the condition of people in the early stages of this disease.

Copolymer-1 (COPAXONE®) was first clinically investigated at the Hadassah-Hebrew University Medical Center in Jerusalem and the Albert Einstein College of Medicine in New York, and follow-up trials were conducted at various other research centers. In a decisive double-blind trial carried out between 1991 and 1994, copolymer-1 was tried on several hundred patients in eleven U.S. hospitals.

Multiple sclerosis is a devastating disease affecting mainly young people approaching the prime of their lives. Approximately 1 million people suffer from it around the world, including some 300,000 patients in the US and an additional 350,000 in Europe.

If not for the scientific research carried out by Prof. Michael Sela, Ruth Arnon and their team at the Weizmann Institute of Science, Teva could not have embarked on its epic path of moving from the laboratory to the market place. In 2002 global sales of Copaxone exceeded \$520 million.

***Boston Scientific Signs Agreement for Advanced Imaging and Navigation Technology***

Boston Scientific Corporation (NYSE: BSX ) the world's largest medical device company dedicated to less invasive therapies announced that it has signed an agreement with MediGuide, Inc., a private company with development offices in Haifa, Israel.

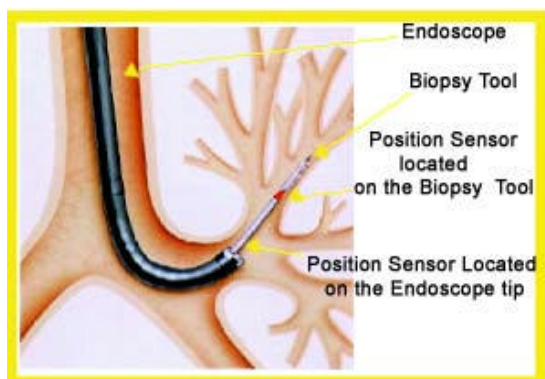
The agreement includes an equity investment in MediGuide by Boston Scientific, co-development responsibilities for integrating Boston Scientific's device platforms with MediGuide's proprietary guidance system, exclusive global distribution and an option for Boston Scientific to acquire MediGuide at a future time.

Elbit Systems Ltd. (Nasdaq:ELST) is a majority share-

holder in MediGuide. Other investors in MediGuide Inc. currently include VitaLife, V.C., The Fishman Group, Docor International and D.O.H. Investment Ltd.

The agreement calls for developing and commercializing of technology platforms in the field of 3-D intravascular imaging and intrabody navigation. The initial focus of the alliance will be on interventional cardiology.

MediGuide has developed an advanced navigation system known as the Medical Positioning System (referred to as MPS), which enables the real time tracking of miniature sensors integrated into therapeutic and diagnostic medical devices. These "MPS ready" devices will allow physicians to accurately track progression of the device as they are manipulated through the human anatomy while continuously registering their exact location and orientation utilizing advanced diagnostic systems such as Boston Scientific's intravascular ultrasound



(known as IVUS) system as well as additional non-invasive diagnostic systems including angiography, magnetic resonance imaging (MRI) and computed tomography scanning (CT).

MPS is designed to monitor the exact location and orientation of a miniature sensor that can be integrated into existing catheter-based therapeutic and diagnostic devices. This technology would more accurately track the location of the device as it is manipulated through the body and delivered to the treatment site.

In addition to opportunities in cardiovascular interventions, the alliance will explore opportunities to develop "MPS-ready" devices in the fields of radiology, neurosurgery, oncology, endoscopy, orthopedics and other medical specialties.

Boston Scientific and MediGuide initially plan to develop a next generation intravascular ultrasound (IVUS) sys-

tem that would provide physicians a three-dimensional intravascular image of coronary arteries by integrating Boston Scientific's IVUS system and MediGuide's Medical Positioning System (MPS). This enhanced imaging capability would help physicians better assess the condition of the artery and treatment options.

### ***Pitango Invests \$1m Serpomed***

BeerSheba based Serpomed Ltd has finalized a \$1million agreement with Pitango Medical Ltd, for the global commercialization of the company's intravenous safety catheter.

Serpomed's intravenous safety catheter provides a simple and highly cost-effective solution to needle-stick problems, commonly occurring among clinical staff.

The worldwide catheter market is estimated at over \$2 billion. In order to prevent AIDS and other diseases spread by contact with blood, many markets including the United States, are now introducing legislation requiring the use of safety products. The Serpomed catheter, with its intrinsic safety features is expected to become a significant product in this market.

The safety catheter is an invention of Dr Sergey Popov, who immigrated to Israel from Moldova, in 1991 and whose other inventions include a surgical stapler, a haemodialysis safety needle and a range of innovative trocars.

Serpomed was founded by Dr. Popov with Israeli investors in 2001. Dr. Popov is the president of the company, with Stephen Jacobs serving as VP business development.

### ***Agis Pharmaceuticals' Profits Soar***

Profit reached NIS 32.3 million (more than \$7.0 million), and exceeded expectations.

Israeli drug maker Agis Industries (TASE:AGIS) reported that its net profit almost quadrupled in the first quarter following a major expansion in its international operations.

Net profit reached NIS 32.3 million, or NIS 1.18 per share, compared with profit of NIS 8.5 million in the same period last year.

"The major source of the higher profits during the quar-

## Israeli Companies on Wall Street

ter was the rise in revenue from the company's international operations, which reached NIS 260.6 million, (\$57

million) a 69% increase in comparison with the same period a year earlier," Agis stated in its first quarter report.

Revenue from overseas sales accounted for 60% of Agis's total sales in the first quarter, which reached NIS 433.2 million. Total revenue rose 30% from revenue a year earlier, which totaled NIS 335.2 million.

The share has soared 70% since the start of the year.

### ***Greek Officials and a U.S.-led group Sign an Olympic Security contract***

Greek officials chose Science Applications International Corp. of San Diego in March after the group made a final offer of 255 million euros (US\$280 million) and won the bid.

The contract calls for the construction and operation of a central security command and communications system for the 2004 Games. Under the deal, Greek industries will produce 100 million euros (\$110 million) worth of equipment.

Major companies in the SAIC consortium include Germany's Siemens AG; General Dynamics of Falls Church, Virginia; New Jersey-based Honeywell International; and the Israeli company Elbit Systems. Several Greek companies are in the group.

The losing bidder was a consortium headed by the French-British company Thales SA and Raytheon, based in Lexington, Massachusetts.

### ***Cadent Raises \$5.3m***

Israeli start-up Cadent has raised \$5.3 million in its fourth financing round. The company's existing investors participated in the round: Pitango Venture Capital, Apax

Partners, JP Morgan Partners, and Schroder Investments. Another investor, Isratech

Venture Capital Fund, did not participate.

Cadent has raised over \$30 million to date. Pitango health care ventures managing director Ruthie Alon said Cadent aimed to raise additional capital this year from new and existing investors to complete development of new products. The current round was needed to hire 15 employees and complete dental surgery products.

Cadent also announced that it had appointed Douglas Stickney as CEO. Stickney founded and ran the Trimeridian gambling treatment center. Cadent founder and former CEO Eldad Taub will henceforth serve as company president.

Cadent develops 3D imaging technology using CAD/CAM digital cameras for orthodontic and crown and bridge surgery. The company is also developing imaging techniques to precisely measure gums before surgery. The company has not disclosed the amount of its sales in the US.

Cadent was founded and registered as a US company in 1994. Based in New Jersey, it maintains a development center in Or Yehuda, Israel, and has 135 employees.

### ***Teva's Q1 profit surges***

Israel-based Teva (Nasdaq:TEVA: ) reported that it earned \$137.7 million, or 50 cents per share, up from \$85.6 million, or 32 cents, in the 2002 first quarter. The company had been expected to earn 46 cents per share, according to the average estimate of analysts polled by Reuters Research.

Teva's revenue jumped 40 percent, reaching \$757.4 million.

The company said sales of Copaxone, its MS drug,

were up 44 percent to \$156 million. Sales also were boosted by new generic drugs: Mirtazapine, an antidepressant; and Amox/Clav, a version of Augmentin, the blockbuster antibiotic from GlaxoSmithKline (GSK: news, chart, profile).

### **PAZ Oil Company Selects Retalix StorePoint Integrated Solution**

Retalix Ltd., (Nasdaq: RTLX) announced that PAZ Oil Company has selected the Retalix StorePoint store solution with integrated fuel and food service modules to be installed in all its fuel stations throughout Israel.

PAZ is the leading fuel company in Israel. The company operates 245 fuel stations as well as 45 convenience stores that operate under the Yellow banner. Retalix StorePoint is currently installed in all Yellow convenience stores.

Retalix StorePoint will allow PAZ to manage its large multi-format sites through a single software solution, supporting stand alone fuel stations, fuel stations combined with food service, fuel management support for both self service and/or an attendant full service forecourt. A new StorePoint feature for PAZ incorporates standard point-of-sale capabilities at the pump, using the pump terminal as the checkout display. This capability allows PAZ employees to sell typical in-store products at the fuel pump. Additionally, Retalix StorePoint supports PAZ fleet management by interfacing with automatic vehicle identification (AVI) devices.

Mr. Moshe Sabag, PAZ's IT Director, said, "PAZ is focusing on the transformation of the petrol station into a center of commercial activities. We have selected Retalix's StorePoint solution because of its ability to support this strategic marketing initiative. The broad functionality offered by Retalix's C-Store and Forecourt solutions, will allow us to provide our customers with added value services and one focal point to many of their commercial needs."

According to Mr. Barry Shaked, CEO of Retalix Ltd., "PAZ will be the first to implement an innovative system from Retalix that allows the attendant to utilize the pump terminal as a Point of Sale terminal selling non-fuel products at the fueling island. Additionally, the PAZ system is also unique in its support for multiple types of tendering options such as Pay at Pump with Credit, Pay at Pump with AVI, and Pay Attendant (cash & credit)."

### **Chief Scientist awards Pharmos 2003 Grant of up to \$4.4m**

Pharmos (Nasdaq: PARS) announced that it was awarded a grant of up to \$4.4 million by the Office of the Chief Scientist (OCS) of Israel's Ministry of Industry and Trade.

The portion of the grant allocated for Pharmos' traumatic brain injury (TBI) program with dexanabinal totaled \$3.1 million, a 24% rise from OCS funding in 2002, Pharmos said. The remaining portion of the 2003 grant is split between development of dexanabinal for prevention of cognitive impairment, and development of proprietary compounds to treat autoimmune and neurological diseases.

The company announced earlier this month that it was "entering into the homestretch" of its Phase III trial of dexanabinal for head injury. More than 580 patients have been enrolled to date in over 60 international centers participating in the trial.

**ISRAEL HIGH-TECH REPORT**  
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JOSEPH MORGENTHAU, EDITOR

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