

Israeli Academia Provides Strong Roots for Biomedical Business Development

Israel's technology transfer companies have enhanced cooperation to provide a one-stop-shop for investors and strategic partners.

Israeli academia provides the fertile soil from which the innovative ideas for the country's life science sector are grown. The country's technology transfer companies (TTCs), owned by Israel's universities, research institutes and medical organizations, provide a seamless and profitable transition from laboratory research to the global marketplace. Israeli academia and medical organizations provide rich research roots for the country's flourishing life science industries in such sectors as biotechnology, pharmaceuticals, medical devices and Ag-bio. Israel Tech Transfer Organization (ITTN), established in 2007 to act as the umbrella organization for Israel's TTCs, recently launched its new website at www.ittn.org.il featuring nearly 1,000 patented projects, which have matured to the point where seed investment is required. The U.S.-Israel Science and Technology Foundation (USISTF) played a major role in initiating the formation of ITTN and support the organization.

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Gaby Kenan, Chairman of ITTN and CEO of Bar-Ilan Research and Development, believes that the cooperation between Israel's TTCs will result in more ideas being transformed into marketable products and solutions. He said, "We are a one stop shop for international companies, VC funds and other investors looking for new Israeli technologies. Our site makes discovering Israeli talent much easier." Bar-Ilan Research and Development Ltd. at Bar Ilan University is one of 12 members of ITTN. The others are: BGN Technologies (Ben Gurion University); BioRap Technologies Ltd. (Rappaport Research Institute of the Technion-Israel Institute of Technology); Carmel-Haifa Economic Corp. Ltd. (University of Haifa); Gavish Galilee Bioapplications Ltd. (MIGAL Galilee Technology Center); Hadasit Ltd. (Hadassah Medical Organization); Mor Research Applications (Clalit Health Services); Ramot at Tel

Aviv University Ltd.; Tel-Aviv Sourasky Medical Center; T3 Technion Technology Transfer (Technion Research & Development Foundation Ltd.) Business Development Unit; Yeda Research & Development Co. Ltd. (Weizmann Institute of Science); and Yissum Ltd. (Hebrew University of Jerusalem).

ITTN represents the interest of its member organizations before the Knesset, government authorities, ministries, agencies, and committees and promotes collaborative efforts between the technology transfer community in Israel and its counterparts around the world. As previously mentioned, ITTN also strives to improve the accessibility of the public (and in particular) to new and innovative research findings and inventions performed at Israel's leading universities and research institutes.

ITTN's new site has a state-of-the-art search engine to find new projects, sorting either by TTC or category. In fact about 805 of these projects are in the biomedical sector including biotechnology and life science, medical devices, diagnostics and pharmaceuticals.

Amir Naiberg, Director of ITTN and CEO of Yeda Research & Development, Technology Transfer from the Weizmann Institute of Science, said that Israeli innovation is in its prime and many global giants are canvassing Israel's academic institutions for their next product. A glance at some of the success stories from Israel's TTCs shows the rewards that can be reaped from timely investment. Yeda at the Weizmann Institute of Science boasts two treatments for Multiple Sclerosis. Prof.

Michael Sela and Prof. Ruth Arnon developed the Copaxone® drug, which has provided a breakthrough in the treatment of Multiple Sclerosis and earned Teva Pharmaceuticals sales of over \$3 billion in 2010 alone. Prof. Michelle Revel developed Interferon for the treatment of Multiple Sclerosis, which through the Rebif® medication earns sales of hundreds of millions of dollars annually for the German pharmaceutical firm Merck Serono.

Profitable pharmaceuticals which have graduated

from the Hebrew University of Jerusalem's Yissum include Exelon® for the treatment of Alzheimer's disease developed by Prof. Marta Weinstock Rosin, and marketed by Novartis with sales of over \$1 billion annually and Doxil® an anti-cancer medication developed by Prof. Yechezkel Barenholz in collaboration with Prof. Alberto Gabizon of Hadassah University Hospital, which is produced and marketed by Johnson & Johnson and generates revenue of more than \$500 million per year.

A new Israeli pharmaceutical, which originated in a TTC is Azilect® for the treatment of Parkinson's Disease. The medication, which was conceived by Prof. Moussa Youdim and Prof. John Finberg of the Technion's Rappaport Research Institute, was developed by the Technion in collaboration with Teva. Since being launched, Azilect's accumulated sales have exceeded \$1 billion.

While pharmaceuticals are the most lucrative of successes, and the longest to nurture, Israel's TTCs have produced many other commercial products.

Yissum has spawned Medgenics, which has developed a mathematical formula that harnesses raw genome data, and is traded on New York's AMEX and London's AIM, while Novogali, based in France has currently 2 drugs in Phase III clinical trials for a drug delivery system to the eye. Another promising Yissum spin off, Avraham Pharmaceuticals is currently running Phase II clinical trials in Europe for Ladostigil, which does not only target symptomatic relief in Alzheimer's disease patients, but also has the potential to slow

progression of the clinical symptoms of the disease.

Over the past year, Yeda signed several significant licensing transactions with: Raptor Pharmaceuticals, to develop a drug for the treatment of Huntington Disease; Enlight Biosciences, for the development of a novel systems biology platform; Cerucell, for the development of a Hepatitis B Drug; Avixenna Pharma, for a device for the treatment of nail fungi; Johnson & Johnson, for the study of snoring and sleep apnea; Prolor Biotech, for the development of long acting medicines.

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The Technion's successful life science offspring includes: Mazor Surgical Technologies, which pioneers miniature semi-robotic bone mounted positioning systems for orthopedic procedures; Regentis Biotechnologies commercializing Gelrin™ - Implantable biodegradable hydrogel matrix for repair of cartilage, bone and other soft tissue applications; and Slender Medical is developing Novel body shaping technology using non-invasive HIFU, including feedback based on temperature and tissue mapping; Applied Immune Technologies (AIT) is developing T-Cell Receptor-Like (TCRL) antibodies for therapeutic and diagnostic applications of cancer and viral diseases; Itamar Medical develops, markets and sells diagnostic medical devices based on PAT™ (Peripheral Arterial Tone) signal and its products include innovative tools for the diagnosis of cardiovascular disease and sleep related breathing disorders; Corindus provides intuitive robotic technologies for catheterization laboratories and radiology/special procedure suites.

Ben-Gurion University's BGN commercializes its novel technologies by out licensing to established companies as well as by creating new start-ups. BGN's licensing includes a 3D alginate scaffold and a novel bioreactor licensed to Life Technologies, a worldwide leader in biotechnology products. BGN's expertise and innovations in microalgae has been the basis of several commercial success stories. Algaetechnologies, a developer of the red pigment astaxanthin and other healthcare related products has been established on the basis of BGU's innovations in the production of high value microalgal products. Israeli's Frutarom is producing and selling to major cosmetic companies microalgae derived polysaccharide compounds developed at BGU and just recently a research and commercialization collaboration with a major Chemical company has been initiated.

BGN's Life Science and Medical Companies include Protea Vaccine Technologies recently acquired by NasVax Ltd. (TASE: NSVX), which develops

an innovative next-generation vaccine against *Streptococcus pneumoniae*; Vacciguard, a developer of vaccines against several pathogens for which there are currently no effective vaccines and therapeutic vaccines against devastating diseases, such as cancer; Amorphical, engaged in the development of synthetic dietary supplements and drugs for treatment of human bone metabolism-related disorders based on unique biomineral derived from crustacean mineral deposition;

CartiHeal focused on a novel and proprietary comprehensive implant for repair of articular cartilage and osteochondral defects and NESS(Bioness) a the producer of HANDMASTER, an FDA approved electrical device that restores function to the paralyzed upper limb and is partially owned by Johnson & Johnson. Additional BGN technologies and innovations are under development by worldwide companies.

Successful life science projects at Tel Aviv University's TTC Ramot include the technology licensed to Allon Therapeutics. Allon has

developed technology to show potent neuro-protective capabilities in a wide range of chronic neuro-degenerative diseases and is currently conducting Phase II/III clinical trial in progressive supranuclear palsy (PSP), a type of frontotemporal dementia (FTD). Ramot has concluded licensing agreements with Wyeth, regarding Alzheimer's disease, immunotherapy, and with a European based company regarding prevention of amyloids aggregation. Another license conducted by Ramot to Concordia Pharmaceuticals has focused on Salirasib, a novel orally effective, targeted well tolerated ras-inhibitor indicated for treatment of a wide range of cancers. Salirasib is currently in Phase II clinical trials as part of an agreement between Concordia and Ono Pharmaceuticals to develop and commercialize the drug in Japan.

Bar Ilan Research & Development Co. (BIRAD) commercializes its technologies via licensing and or R&D agreements both to established companies and start-ups. BIRAD has licensed to BioLineRx, BL-6010 – an insulin secretagogue for type II diabetes, and a novel compound for treatment of glaucoma, which

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has entered BioLineRx's Early Development program. In addition, BioLineRx reported it has signed a \$365 million out-licensing deal with Cypress Bioscience for the antipsychotic drug BL-1020, which was licensed from BIRAD and Ramot.

BIRAD has also concluded a licensing agreement with NanoThera Ltd., granting the start-up an exclusive license for development of nano-pharmaceutical drugs. Additional agreements with start-up companies include licenses in the field of personalized medicine for treatment of leukemia (in collaboration with Tel Aviv Sourasky Medical Center); development of male contraceptives; development of diagnostic kits for sperm, and development of an enhanced radiosensitizer in the framework of therapy for cancer.

Pipeline projects currently underway include development of prodrugs in the field of multiple sclerosis, Alzheimer's, therapeutic protein design, rapid sequence alignment for use in personalized medicine, molecular medical imaging, and biosensors.

Hadasit, Hadassah University Hospitals' commercial arm, has gained global recognition for successfully enterprising biomedical technologies developed at Hadassah. Several products based on Hadasit technologies were launched in recent years, including Doxil® and Periochip (in collaboration with Yissum), Travelan (by Immuron Ltd.) and 13C-Urea BreathID (by Exalenz Ltd.). Hadasit took a major step in 2006 when it held a public offering on the Tel Aviv Stock Exchange of Hadasit Bioholding Ltd. (HBL), representing seven of the start-up companies in Hadasit. The companies are in various stages of developing products focusing on stroke, oncology, regenerative medicine and inflammatory disease. In 2010, Hadasit portfolio companies including Thrombotec, Enlivex, BioMarCare, Exalenz, Biokine and NasVax performed clinical trials based on Hadasit technologies, and raised over 70 million NIS. Another initiative is the collaboration of Hadasit with Bezalel Academy of Arts and design to develop medical and para-medical products that will answer the needs of patients and healthcare providers.

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Hadasit is also a partner in BioLineRx together with Teva Pharmaceuticals, Pitango Venture Capital, Giza Venture Capital and the Jerusalem Development Authority. BioLineRx is developing proprietary drugs for the treatment of schizophrenia, neuropathic pain, and damaged caused by acute myocardial infarction (heart attacks). Hadasit and the HBL companies have moved into the Jerusalem BioPark located on the Hadassah Ein Kerem medical campus.

The BioPark is also home to the Hadassah Clinical Research Center - a GCP-compliant, 15-bed unit offering pharma, device, and biotech companies a complete package of services and facilities for conducting Phase I and II clinical trials.

The Medical Research Fund of Tel Aviv Sourasky Medical Center is looking to commercialize, among other things, a novel carrier for the delivery of drugs to the brain, antibodies against CD24 for treatment of colon cancer, as well as devices such as a tool aimed at improving the gait of the elderly population, and a system for treating glaucoma.

Mor Research Applications, the TTC of Clalit Health Services,

offers a wide portfolio of medical devices, diagnostics and pharmaceutical projects based on the innovative and evidence-based ideas of experienced Clalit clinicians. Mor serves over 7,500 physicians in 14 hospitals throughout Israel. Mor's spin-offs include companies such as Prolor (Nasdaq), enhancing the in vivo potency and longevity of peptides; CureTech (TASE), developing novel, broad-spectrum, immune modulating products for the treatment and control of cancer; MGVS, which develops therapeutic products for heart and blood vessel disorders; Angioslide, developing the next generation of balloon angioplasty catheters; MinoGuard, a phase II company developing innovative drug combinations for schizophrenia; and, MediWound with Debrase® Gel Dressing (DGD), an effective burn wound debridement agent. MediWound has recently closed a significant license agreement with Teva Pharmaceuticals.

Mor is currently seeking to commercialize projects in the areas of cancer, schizophrenia, osteo-arthritis, genetic diagnosis for heart failure,

cardiovascular, cancer, ophthalmology, ENT, surgery and herbal medicine.

Carmel - Haifa University Economic Corp. has Ag-Bio projects including the development of salt-stress tolerant organisms and transgenic plants containing a drought resistant dehydrin gene. In addition Carmel suggests various diagnostic methods and tools, among them a method that uses handwriting process measures and supplementary self-report questionnaires as a system for analyzing human dysfunctions. The method has applications in diagnosing Alzheimer's, attention deficit hyperactive disorder (ADHD), multiple sclerosis (MS), and depression; additional diagnostic tool for Parkinson's disease was developed by an interdisciplinary team of researchers from Computers Science and the Institute of Evolution. They developed a novel computerized system for automatic quantification and measurement of Time-Space patterns of facial features during facial expression. The system is intended as a monitoring and decision support tool for the detection and progression evaluation of medical disorders that affect the performance of facial muscles, and currently it is exploited in a study on Parkinson Disease; In addition, BioHug which has graduated from Carmel, developed a device which is a non-restraining, drug-free method to calm individuals in distress. The device is a vest that delivers mild pulsating pressure through the use of inflatable cells placed throughout the garment. Moreover, Carmel offers to commercialize four unique pharmaceutical projects: a) a technology (patent pending) dealing with Regulation of Neuronal Translation as New Therapy for Neurodegenerative Diseases (Cognitive Enhancer); b) a novel anti cancer drug technology based on ARTS-mimetic; c) Novel Steroidal Hormone Antagonists; d) Technology of using the cell-substrate impedance sensing system for the evaluation of macrophage pro- and anti-inflammatory responses. Also in the north, the Migal Galilee Technology Center in Kiryat Shmona, houses a range of projects

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in therapeutics, diagnostics, AgBio and medical devices. These include a cancer immunotherapy project, drug discovery and the development of an automated rapid bench-top DNA sequencing device. Migal, together with private investors and the Galilee Development Corporation, established an investment company in the field of medical devices. The new company invests in early stage projects that operate within Migal's premises in Kiryat Shmona. Migal's development team will reach the proof of concept stage within a short time.

In Haifa the Rappaport Family Institute for Research in the Medical Sciences has established BioRap Technologies, which is developing a range of projects including novel molecules as potential drug candidates, biomarkers and diagnostic kits for cancer, coagulation disorders, diabetes and neurodegenerative disorders. In particular, Rappaport has developed Vaccinogen - a platform technology for the discovery of new therapeutics for autoimmune and cancer disease. BioRap spin-off companies include Plexicure a start-up company which develops a drug for cancer; Iluten, developing drugs for inflammatory autoimmune diseases; Microrap, which develops a novel diagnostic kit for Type 1 Diabetes and Haptocure a new start-up company for developing drugs and a diagnostic a pharmacogenomic kit for preventing Type 2 Diabetes complications.

Other TTCs in Israel, which are not members of ITTN include Israel's government-owned medical centers and research institutions. Among these are Kidum - Agricultural R&D Applications Unit, the TTC of the Ministry of Agriculture's Vulcani Institute Agricultural Research Organization (ARO), which handles 70% of all agricultural research in Israel. Another such TTC is Jerusalem College of Technology/Ninbar, which has developed an innovative automatic blood pressure meter. Israel's TTCs have an impressive track record provide new technologies to the world's leading corporations. Now boosted by the activities of ITTN, more ideas are more easily available to the global business community.