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Biotech - Tailor-made for Israel

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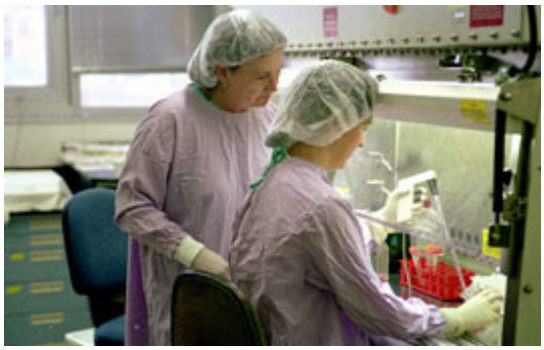
Israel creates more medical devices per capita than any other, and earns $3 billion a year from biotech - it's an innovative and skilled industry that suits the country perfectly.



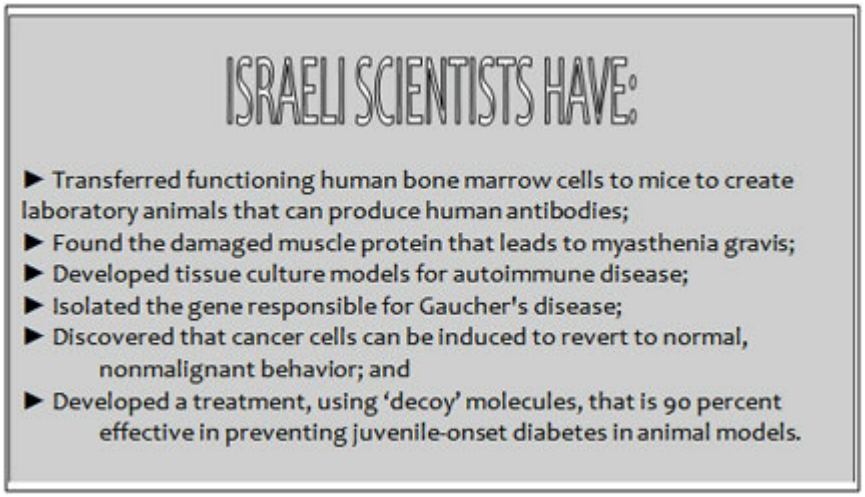
Scientists throughout Israel's universities and hospitals are developing innovative new biotechnologies. (Photo courtesy Hadassah Medical Center)

Blockbuster prescription drugs sold worldwide that treat multiple sclerosis, cancer, Alzheimer's and Parkinson's diseases derive from Israeli biotechnology. Israel creates more medical devices per capita than any other country, and its life sciences exports earn more than $3 billion a year.

Israeli research is at the forefront of the emerging fields of stem-cell therapy and genomics, and two Nobel Prizes in Chemistry, the first to Profs. Avram Hershko and Aaron Ciechanover of the Technion-Israel Institute of Technology, and the second to Prof. Ada Yonath of the Weizmann Institute of Science number among the many awards bestowed on the country's biotech scientists.

Israeli professor Ada Yonath, who won the Nobel Prize in chemistry in 2009, for her work in stem cell research (Photo courtesy Weizmann Institute of Science)

The pace of innovation, development and growth in Israel's biotechnology sector is unparalleled. Israel's biotech industry is the most aggressive in the world, with more startups per capita then any other country. Its 180 biotech companies - each built on a combination of academic excellence, a highly-skilled workforce, cutting-edge technological inventiveness and entrepreneurial daring - are creating therapeutic products, diagnostic tools and revolutionary drug-delivery techniques benefiting people all over the world.



Tailor-made for Israel

Biotechnology, the science which applies breakthroughs in molecular biology and immunochemistry to diagnosis and therapy, was born in the late 1970s. In many ways, it is tailor-made for Israel, being rooted in innovation and perseverance; a highly educated workforce; the lessons of military service; intimate links between researchers and entrepreneurs; and US capital and markets and, particularly, the US 1985 free trade agreement with Israel.

• Innovation and perseverance: A small country with a population of only seven million and few natural resources, Israel's economy is necessarily one of innovation and perseverance. Demanding conditions - first in agriculture, then in defense and from there throughout its economy - set the stage for dramatic economic growth, as Israel transformed itself from a developing to a developed nation, and from an economy based on agriculture to one based on knowledge.

• A highly educated workforce: With seven world-class universities, Israel is one of the most highly educated countries on the globe. Almost a quarter of its workforce has university degrees, and 12 percent of these have advanced degrees. Among the 750,000 people who immigrated to Israel from the Former Soviet Union between 1989 and 1991 were hundreds of highly skilled engineers. They have enhanced Israel's technological talent pool, giving the country the world's highest rate of scientists per capita (one in 200), 39 percent of whom specialize in life sciences.

• The lessons of military service: Mandatory military service in Israel equips its young people with the connections, management skills and action-oriented entrepreneurial mindset critical for technological development.

• Intimate links between researchers and entrepreneurs: Israeli universities were among the first worldwide to develop technology transfer organizations - professional companies tasked with helping Israeli researchers to commercialize their academic research by connecting them with national and multi-national companies.

• US capital and markets and, particularly, its 1985 free trade agreement with Israel: The US as a trading partner helped fuel the high-tech boom of the 1980s and 1990s, which, in turn, created the conditions for Israel's biotechnology cluster.

Birth of biotech in Israel

Israel whimsically dates the birth of its biotechnology industry to 1936. This was when chemist Chaim Weizmann, later to be the country's first president, developed a process that produced acetone from the bacterium Clostridium acetobutylicum. It took almost six more decades, however, until the modern Israeli biotechnology industry was born, on the heels of the high-tech boom.

While Israeli biotechnology embraces the whole biotech sphere - from animal vaccines and diagnostics to plant tissue culture, bioreactors, seeds, diagnostics and biopesticides - its emphasis is firmly on medical agents, diagnostics and cell- and tissue-therapies. Some 60 percent of Israeli biotech focuses on human therapeutics, including drug discovery, cell therapy and genetics. A further 20% of Israeli biotech companies produce diagnostic kits.

Top-selling prescription drugs based on Israeli research

The best-known and most successful medication developed in Israel is Copaxone®, a breakthrough treatment that significantly reduces the severity of clinical episodes in multiple sclerosis patients, also making them less frequent. Developed by Teva Pharmaceutical Industries and the Weizmann Institute of Science, it is the world's leading MS therapy, approved in 52 countries, with global sales reaching $2.8 billion in 2009.

The most successful medication developed in Israel is Copaxone, by Teva Pharmaceutical Industries, which is used to treat multiple sclerosis.

Teva's first proprietary drug, Copaxone®, is today responsible for a third of the company's profits. Teva is one of the 15 biggest international pharma companies in the world and one of the largest generic drug manufacturers. The company employs more than 35,000 people in 50 countries, and earned almost $14 billion in 2009. It is increasingly expanding into cutting-edge patentable therapies.

Ailect® (rasagiline) is another Teva product. Based on research at the Technion Institute of Technology, it combats Parkinson's disease, both as initial therapy and, later in the disease, in conjunction with L-dopa. Its 2009 sales reached $175 million.

Azilect, which is used to treat Parkinson's disease, was based on research from the Technion Institute of Technology. (Photo courtesy of H. Lundbeck A/S)

Exelon® is a medication for Alzheimer's disease that reduces symptoms, enabling patients to remain independent and 'themselves' for longer. Originating in research at the Hebrew University and developed and commercialized by Novartis, its global sales in 2009 were more than $954 million.

Doxil® is a chemotherapy agent used in treating different types of leukemia, Hodgkin's lymphoma, multiple myeloma and cancers of the bladder, breast, stomach, lung, ovaries and thyroid. Based on research at the Hadassah Medical Center, it was sold to Johnson & Johnson, and recorded global sales of $430 million in 2009.

Regenerative Medicine

Scientific regulation in Israel is informed by Judaism's emphasis on the saving of life. The country's relatively liberal approach to stem cell research for therapeutic purposes derives from this tradition, which has positioned Israeli scientists among stem-cell research's pioneers and kept them at the heart of the regenerative medicine map, helped by a government-sponsored research consortium spanning academia and industry. While no stem-cell medication yet exists anywhere, several are on the way from Israeli companies.

The four-year-old Jerusalem start-up Cellcure Neurosciences is starting clinical trials in patients with age-related macular degeneration (AMD), the leading cause of blindness in over-50s in the Western world, which is estimated to affect some 30 million people.

The disease is caused by the dysfunction, degeneration and death of pigment-including retina cells, which lie between the retina's photoreceptors and the nourishing blood vessels at the back of the eye. Cellcure creates healthy retinal pigment cells from human embryonic stem cells, and injects them into the eye to replace the dying cells.

Jerusalem-based Gamida Cell has developed stem cells from umbilical cord-blood to treat blood cancers, autoimmune diseases, metabolic disorders and the hematological disease neutropenia. Its lead product is StemEx, which was given FDA Fast Track Designation in mid-2010. It is now being tested in international Phase III clinical trials as an alternative to bone marrow transplant in patients with advanced blood cancers, who are unable to find a matched donor.

BrainStorm Cell Therapeutics in Petah Tikva is a leading developer of adult stem cell technology and therapy. It has created a stem cell treatment for patients with amyotrophic lateral sclerosis (ALS or Lou Gehrig's disease) and Parkinson's disease based on autologous bone-marrow-derived adult stem-cells. In a first clinical trial, conducted at the Hadassah Medical Center, ALS patients will be re-implanted with stem cells taken from their own pelvis.

Drugs derived from living cells

Uplyso, a medicine for Gaucher's disease based on the enzyme taliglucerase alfa, is an example of the ongoing push into biologics - drugs derived from living cells rather than from chemicals. It was developed by Protalix Biotherapeutics, a company that began life in 1994 within Israel's Meytav Technological Incubator, graduating to become an independent publicly held company with a market capitalization of more than $700 million, trading on both the NYSE Amex Exchange and the Tel Aviv Stock Exchange.

It recently sold the rights to this experimental Gaucher's medication for $60 million to the New York-based Pfizer, the world's largest-selling pharmaceutical firm.

Neuroprotective drugs

D-Pharm Ltd. (TASE: DPRM) is focused on the design and development of innovative drugs for the treatment of serious, potentially life-threatening medical conditions that affect the brain.

The Company has developed two unique platform technologies that generate lipid-like medicines. These technologies use cell-membrane specific mechanisms and influence lipid-related biochemical pathways, for therapeutic effect.

The Company has two products in advanced clinical development: a Phase III product, DP-b99, for treatment of acute ischemic stroke; a Phase II product, DP-VPA, for the treatment of complex partial epilepsy, migraine and bipolar disease. D-Pharm is an integrated drug development organization with headquarters, research and development laboratories, and pilot manufacturing plant in the Kiryat Weizmann Science Park, Rehovot.

Computational Biotechnology


Martin Gerstel, chairman of the board at Israeli computational biotech company Compugen, and a major figure in Israel's biotech industry.

Compugen is a leading drug and diagnostic product candidate discovery company. Unlike traditional high throughput trial and error experimental based discovery, Compugen's discovery efforts are based on in silico (by computer) product candidate prediction and selection utilizing a broad and continuously growing infrastructure of proprietary scientific understandings and predictive platforms, algorithms, machine learning systems and other computational biology tools to address important unmet therapeutic and diagnostic needs - either for Compugen or its partners.

Compugen's growing number of collaborations covering the further development and commercialization of Compugen discovered product candidates all provide Compugen with potential milestone payments and royalties on product sales or other forms of revenue sharing. These collaborations may be entered into before product candidate discovery is undertaken pursuant to "discovery on demand" type arrangements, or with respect to existing product candidates, collaborations can be initiated prior to or at the proof of concept stage, or after additional preclinical activities have been undertaken by Compugen.

Genomics

Genomics uses the RNA system within living cells to control which genes are active and how active they are. Rosetta Genomics, based in Rehovot, is using RNA-based technology to develop a wide range of diagnostic tests for cancers and women's health indications.

Quark Pharmaceuticals has created a fully-integrated drug development platform to deliver RNA molecules to the eye, ear, kidney, lung, spinal cord and bone marrow, where they can block the action of faulty genes.

Diagnostics

Diagnostics, particularly monoclonal antibody-based test kits, were among Israel's first commercial biotechnology successes. Aided by Israel's vast clinical medicine resources, new diagnostic tests are brought rapidly from the lab into the hospital ward and to market. Savyon Diagnostics was an earlier entry in this field in 1983, when Ben-Gurion University researchers developed a serological diagnostic kit to test for the sexually transmitted

disease Chlamydia ('clap').

They formed the company a year later, and brought their test-kit to market in 1989. Savyon has gone on to develop and market tests for urinary tract infections and for HIV.

Orgenics, founded in 1983, produces 22 patented easy-to-use, stand-alone, ELISA-based ImmunoComb kits that test for Chlamydia, hepatitis A and B, cytomegalovirus, toxoplasmosis, rubella, Helicobacter pylori and AIDS, as well as non-wipe strips for measuring blood glucose levels.

Zer Science-Based Industries specializes in diagnostic tests related to fertility. Its Single-Step pregnancy test requires just drops of urine to give an accurate result within five minutes, even before the first missed menstrual period.

Future blockbusters

One example among many is Glassia, the first and only high purity, liquid, ready-to-use α1-proteinase inhibitor for adults with inherited emphysema resulting from α1-antitrypsin deficiency.

Kamada, the 20-year-old biopharmaceutical concern that invented Glassia, entered an exclusive distribution and manufacturing agreement for its production in mid-2010 with the global health-care company Baxter International.

Biotech and electronics

One of the best-known diagnostic devices developed in Israel is the Pillcam, created by Given Imaging. The pill-sized camera can be swallowed, and is used to diagnose stomach disorders.

Among Israel's strengths is the interdisciplinary nature of its R&D. This underlies the creation and development of out-of-the-box products. One of the best-known and among the most important and successful life sciences developments to come out of Israel in the past decade, is the Pillcam from Given Imaging, a disposable pill-sized camera encased in a capsule and used to diagnose stomach disorders after being swallowed.

Easily ingested, the capsule moves naturally and painlessly through the gastrointestinal tract, wirelessly transmitting to a portable recorder as it goes, to provide the physician with high-quality images on a computer workstation.

Financing Israel's biotech

Israel's biotechnology track record is strong. Companies that have commercialized their products and been publicly listed do exceptionally well - testifying to their excellent science.

The process of scaling up biotech R&D to early production and beyond, however, is a high-risk undertaking. With only one in 250 compounds making it from preclinical development to market (and taking perhaps seven years and $500 million to do so), the major brake on Israel's biotechnology cluster is the lack of an asset-intensive infrastructure.

Investment is in especially short supply for the so-called Valley Of Death phase - the gap between very early stage investment (usually academic research funds), and easier-to-obtain investment for the clinical study phase which, although more costly, is correspondingly more certain than early-stage technologies.

Government help

Israel's government supports a spectrum of programs to help start-ups survive the difficult stages between proof of feasibility and final success. They include R&D grants from the Chief Scientist's Office (since the early 1990s); the Magnet framework that brings companies and researchers together to develop novel generic technologies, underwriting up to 65% of the budget (since 1994); a National Committee for Biotechnology tasked with developing and promoting biotechnology in Israel (established in 1995); Bioplan 2000, which created dedicated biotech incubators to bridge the gap in funding, infrastructure and managerial talent; naming biotechnology a National Project and creating infrastructure centers which give researchers access to essential equipment and knowhow (2002); and, most currently, a generous Grants Program administered by the Israel Investment Center; an Automatic Tax Benefits program administered by the Tax Authorities, offering foreign investors unique advantages; and finally, deignating biotechnology a Preferred Sector.

Academic research funding

Israel's biotech research at its universities and medical schools is the foundation of the industry. Dedicated biotechnology departments are rare anywhere, but there are three among Israel's seven main universities. Biotech research is funded from the annual $140 million research budget at Israel's universities and is comprised of external competitive research grants (36%); the regular budget of the universities (36%); and industry and government research grants and contracts (28%).

Technology transfer

Israel has 12 technology transfer organizations, seven of them university-based and five in its leading research hospitals. They are highly effective: the Hebrew University's Yissum, for example, founded in 1964, generates more revenue than its counterparts at MIT, Harvard or NYU in its management and licensing of thousands of patents developed within the institution. More successful still is the Weizmann Institute's Yeda, which has been named the world's third most profitable technology transfer organization.

Incubators

Based on Israel's high-tech experience, incubators have been created to nurture young biotech companies. There are both public and private incubator organizations, but all offer fledgling entrepreneurs skilled and experienced management, suitable R&D facilities, technical, financial, administrative and logistic support, administrative services (secretarial, accounting, legal, acquisition) and business guidance.

The Technological Incubators Program, established in 1991 for high-tech and administered by the Chief Scientist's Office, includes a number of biotech startups. BiolineRx was set up in 2003 by Teva, Hadassah's technology transfer company Hadasit and two leading venture capital funds as a clinical-stage, publicly-traded, biopharmaceutical development company. It licenses promising early-stage projects and develops them as far as Phase I clinical trials.

Rad-Biomed Accelerator is another interface between biomedical research and Israel's biomedical industry. It provides physical infrastructure, seed capital, business development and a wide range of related services to help entrepreneurs establish companies that will join the flourishing Israeli biomedical industry.

International partners

Throughout most of biotech's history, small companies have been the hotbed of innovation. These small firms, however, generally lack the development capital to fund the costly clinical trials and launch of new therapeutics. Biotech has, therefore, long depended on partnerships with large, profitable pharmaceutical companies.

For Israel, this paradigm means that the fruits of Israeli research go largely to foreign companies - with the large partner selling the final product and capturing the lion's share of the profits.

The unraveling of interferon's mechanisms and isolation of the human Interferon-beta gene, for example, which began at the Weizmann Institute, was eventually sold to Swiss pharmaceutical giant Ares-Serono Group in 1979.

Growing numbers of Israeli companies today, however, are searching for funding that will allow them to develop their own intellectual property, rather than sell to the multinational pharmaceutical companies.

Venture capital

Israel's venture capital (VC) industry, born in the late 1980s, received a major boost in 1993, when the government launched the company Yozma to help finance high-tech and, later, biotech startups.

During the 1990s, local venture capital companies that specifically targeted biomedicine were formed. Medica, Columbine, Innomed of Jerusalem Global Ventures, Denali and Vitalife were among the first. ontifax, 7 Health Ventures and Poalim Medical III followed.

With most of these funds now fully invested (or no longer active), local investment in life sciences today comes largely from general VCs, not dedicated to biotech.

Clal Biotechnology Industries (an Israeli investment company but not a VC) has a portfolio of 16 young biotech firms. A number of foreign VC investors have targeted Israel's life sciences in recent years - among them NGN Capital, Onset Ventures, Schroder Ventures Life Sciences, Three Arch Partners and Ziegler Meditech Orbimed, a US firm that invests in the healthcare sector and has been active in Israel for the past decade, expanded its investment team into Israel in April 2010.