Microeconomics of Competitiveness

Israeli Biotechnology Sector

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EXECUTIVE SUMMARY

In the almost six decades since its founding, Israel has experienced dramatic economic growth, transforming the country from a developing to a developed country. Beginning with limited infrastructure and natural resources, Israel has transitioned from an economy based on agriculture to one based on knowledge, and is generally considered a prosperous and democratic state, even as it works to remove some of the bureaucratic legacy of its socialist history. This success has been achieved in the shadow of conflict; Israel remains isolated from its neighbors and security is a constant concern.

The excellence of Israel’s universities and the quality of their research in the life sciences provide the basis for a vibrant biotechnology industry. Indeed, biotechnology sector is often referred to as one of the brightest “stars” in Israel’s technological galaxy.

While the Israeli biotechnology cluster has certainly experienced dramatic growth in the number of firms over the last 10 years, the majority of firms are small and are struggling to commercialise basic research from universities. The challenge for the cluster is, therefore, to enhance the conversion of university research into commercial products.

Greater commercialisation of basic research requires action by the government, institutes for collaboration and individual firms. The government must assist firms in bridging the funding gap between basic research and venture capital funding, and additionally develop the pool of managerial talent in biotechnology. Institutions for collaboration (IFC) must take a more active role to lobby the government to remedy Israel’s divergent intellectual property law. Firms must assume greater responsibility for communicating the needs of the industry to the IFCs and the government. Such steps, among others, are vital if Israel is to realize the potential of the biotechnology cluster.
1. COUNTRY ANALYSIS

1.1. Overall Economic Performance

Over the past 58 years, Israel’s economy has grown dramatically, with GDP per capita increasing by 3% annually, from below $5,000 to $26,300 today (see Exhibit 1). Remarkably, this growth has occurred despite a hostile neighborhood and a conflict-ridden history, including five wars against its Arab neighbors since 1948 and ongoing disputes along multiple borders.

Exhibit 1: Israel GDP / Capita (in 2005 USD)

Israel’s geopolitical situation has shaped its dramatic economic growth. A small country of only ~7MM people, Israel is a land of immigrants; even today only 41% of Israeli citizens were born there. From the early 1900s when Palestine was a British mandate, an early wave of immigrants came from Eastern Europe and Russia, fleeing persecution and motivated by a Zionist socialist vision of a Jewish homeland. These Halutzim, or “pioneers,” promoted collective enterprises on agriculture-based settlements, kibbutzim. As a result, even though much of the country was desert, with perseverance and the development of innovative drip irrigation technologies, the country become agriculturally productive, with crops including citrus fruits. These demand conditions laid the groundwork for the later development of an agro-technology cluster.

At the same time, these immigrants, many of whom were skilled, established universities, laboratories, and companies. For example, Technion, Israel’s Institute of Technology which is still

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<th>Basic Facts about Israel</th>
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<td>Founded:</td>
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<td>Population:</td>
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a pre-eminent institution, was founded in 1912, the Hebrew University of Jerusalem in 1918, and the Weizman Institute of Science in 1949. Some immigrants brought their trades with them, including diamond cutting and polishing, which even today is one of Israel’s biggest exports. Waves of immigration accelerated after World War II and the Holocaust, leading in 1948 to the foundation of the state. The Law of Return, passed in 1950, provides automatic citizenship to any Jewish person.

After 1948, ongoing conflict with neighboring countries led Israel to a policy of self-reliance for defense needs, particularly after the French arms embargo following the 1967 Six Day War with Egypt, Jordan, and Syria. Faced with strong local demand conditions, a cutting-edge defense industry developed, which remains a mainstay of Israel’s economy (see Exhibit 2). Mandatory military conscription led to the development of other high technology products, often based on civilian applications of technology originally developed for the military. A massive wave of ~750,000 immigrants (13% of Israel’s population) from the Former Soviet Union from 1989-1991, including many highly skilled engineers, further contributed to the technically-oriented talent pool. Increasingly, Israel’s partnership with the U.S., which has highly aligned cultural and geopolitical interest in maintaining a democracy in Middle East, provided capital for R&D and a market for products, particularly after a free trade agreement in 1985. The U.S. relationship also helped improve local competition through the presence of multi-national corporations such as Digital Equipment, IBM, Intel, and Motorola, which were in Israel as early as the 1970s. Together, these conditions fuelled the development of high-tech in the 1980s and 1990s, and created conditions favorable to the development of the biotechnology cluster.

Exhibit 2: Impact of Geopolitical Situation on Economic Activity
In part because Israel is such a small domestic market, exports have of necessity been a key driver of the economy – historically in agriculture and diamonds, and currently in high tech. As Israel’s most important partner, purchasing 28% of Israel’s exports, the U.S. is essentially Israel’s “virtual neighbor.” Other trading partners are the E.U. (33% of exports) and Asia (16%), as well as Latin America (4%) and the rest of Europe (6%); the rest of the world is the remaining 13%. Over the past decade, Israel’s exports have gradually been upgraded toward high-technology goods, which now represent 33% of industrial exports (see orange circles in Exhibit 3). Biopharmaceuticals are a small but growing sector with $1B in exports (3.4% of all exports).

In many fairly evident ways, the Israeli-Arab conflict has constrained Israel’s economic growth by preventing trade with its Arab neighbors. Heightened conflict was, for example, a contributing factor to the economic slowdown between 1973 and 1985. It took the start of the Middle East Peace Process in 1991 to stimulate more significant foreign investment and tourism. Instability has led Israel to engage in activities that could be done more economically elsewhere, and forced significant defense spending – 9% of GDP is spent on defense today, down from about 25% in the
1970s. The conflict has also contributed to high unemployment and economic inequality for Arab Israelis and Palestinians which has, in turn, arguably exacerbated the conflict.

But at the same time, the conflict has also helped spur Israel’s economic development. The conflict led to the creation of the Israel Defense Force (IDF) and mandatory military service for two or three years. The IDF provided a training ground for entrepreneurs by selecting the best math and science high school graduates, and giving them experience with the cutting-edge technology developed through its significant military investments. Israel allowed some technology to be used in civilian applications, and many innovative high tech products were developed by entrepreneurs after leaving the military, often collaborating with others in their tight army alumni networks.

The conflict also cemented Israel’s close economic and military relationship with the U.S. given mutual geo-political interests as well as cultural and historical ties, including the Jewish diaspora in the U.S. Since the mid-1970s, the US has provided about $3B/year in aid, about $2B in security assistance and $1B in economic assistance, although a plan was developed in 1998 to phase out the economic portion of the aid, reducing it by about $120M every year. The Jewish diaspora around the world, much of it in the U.S., contributes about $850MM a year to Israel through philanthropy. Equally importantly, the U.S. and Israel have developed bilateral foundations dealing with economic, security, science and technology, and education issues. The countries have extensive military collaborations, including joint military research, planning, and combined exercises.

Although Israel’s economy has remained strong, from 2001-3 GDP per capita shrank by about 2%. This slowdown, which was greater than in other developed economies, reflects the Israeli economy’s dependence on the security situation and the performance of the high tech sector. The second intifada, which began in 2000, negatively impacted tourism and reduced FDI from $5.1B in 2000 to $1.8B in 2002. Exports were also hurt by the burst of the high tech bubble and U.S. recession. Since 2004, the economy has picked up, with 2.5% GDP per capita growth.
1.2. Assessment of the National Business Environment

In its short history, Israel has developed a sophisticated modern economy conducive to business. The strengths of the national business environment have been driven by factor inputs, as well as government policies that facilitated a positive context for firm strategy and rivalry (see Exhibit 4). While Israel’s GDP per capita is rated 26th in the world, the country has a strong competitive advantage in four areas. Three are factor conditions: quality of scientific research institutions (rated 4), venture capital availability (5), and university/industry research collaboration (11); and one area is part of the context for firm strategy and rivalry: intensity of local competition (9).

**Exhibit 4: Israel’s National Diamond**

The strength of Israel’s factor inputs is driven by a pervasive entrepreneurial approach which, combined with a highly skilled workforce, has created a high level of innovation. Life in a country rife with conflict has led to an aggressive, action-oriented entrepreneurial mindset. Moreover, Israel has the highest percentage of engineers in the world – at lower labor costs than in the U.S. – as well as the highest number of physicians per capita. It rates fourth in the world in generation of annual patents / MM capita at 151, behind the U.S. (287), Japan (277), and Switzerland (173); generates a similarly high proportion of scientific and technical articles; and spends more on civilian R&D as a percentage of GDP (3.5%) than any other country. Israel also has the highest per capita spend on
education, and 35% of young people hold academic degrees from universities in Israel and abroad. Universities have tight relationships with industry that facilitate commercialization of laboratory ideas. Capital is available both from local venture funds and from U.S. sources, including venture funds, corporate investment, and capital markets. Israel has the second highest number of companies listed on U.S. stock exchanges of any foreign country (after Canada).

As a result of these factor inputs, a highly competitive context for firm strategy and rivalry has evolved. Israel is second in world in high tech start-ups, and about 15 percent of all new Internet technologies are developed in Israel. Both Israeli government incubators, as well as the presence of U.S. multinationals, have helped fuel the level of competition.

Demand conditions have not been a major factor in the business environment, although unsurprisingly there is relatively sophisticated demand for technology, with the highest number of mobile phone subscribers per 1,000 people in the world.\(^9\) The country has a high level of computer, and internet penetration. In terms of related and supporting industries, the quality of suppliers is fairly good, but there are relatively few of them.

Overall, the government has contributed to the creation of a good business environment – through macroeconomic, political, and social reform, economic development, and especially cluster development. However challenges remain in most of these areas, partly due to the country’s socialist legacy. The Labor party, which dominated from the 1920s under David Ben-Gurion until the late 1970s, has evolved into a socially moderate party under leaders like Shimon Peres. However Histadrut, the biggest labor federation with 700,000 members – and, until changes in 1994, one of the country’s largest employers – continues to provide a strong labor voice, threatening and every several years implementing general strikes due to budget cuts and pension reforms.\(^{10}\)

From a macroeconomic perspective, the evident failure of the country’s socialist policies from 1973-85, when hyperinflation topped 445%, has led successive governments to pursue policies aligned with the Washington Consensus.\(^{11}\) However deregulation and disengagement from business activities have been slow.\(^{12}\) The government is slowly reducing tariff barriers consistent with WTO
standards, particularly in agriculture and apparel, but trade barriers remain a mild competitive
disadvantage (rated 33 vs. 26 overall). In 2005, the capital market was reformed to separate the
banking system from any involvement in fund management. Last year Israel also officially adopted
a floating exchange rate, formalizing the de-facto floating exchange of the previous eight years.

Politically, the country has a strong parliamentary democracy, but recent events and the system
of proportional representation create uncertainty and slow reform given the perpetual need for
coalition governments. Sudden changes – whether the assassination of Prime Minister Rabin in
1995, the start of the Second Intifada in 2000, or the election of the right-wing leader Sharon (Likud
party) in 2001, and then his recent illness – have made the situation more volatile. The centrist
Kadima party, which won elections in early 2006, is one of twelve political parties and holds 29 of
120 seats in the Knesset, Israel’s Parliament.

Socially, Israel’s absorption over 750,000 immigrants from the former Soviet Union in the
1990s is in part a positive story of integrating skilled engineers who helped fuel economic growth.
But it is also a story of troubling – yet widening – inequalities, particularly for unskilled immigrants
and Arab Israelis. Unemployment is high (8.9%) due in part to continued immigration from
countries like Ethiopia, although it has steadily decreased (10.7% in 2002) in an environment with
increasing real wages (+4.2% in 2005, as of October).

The government has also made some progress on upgrading the business environment. The
Israel Antitrust Authority, with powers comparable to equivalent entities in the US, ensures
competitiveness. The country has also protected intellectual property, although it has been
relatively slow to comply with WTO Agreement on Trade Related Aspects of Intellectual Property
Rights (TRIPS). To spur economic development, the government has encouraged relationships
with other technologically innovative countries through free trade agreements including with the US
in 1985 (the U.S.’s first free trade agreement with any country) and Europe.

However on the negative side, bureaucratic red tape gets in the way of efficiency, and is Israel’s
biggest competitive disadvantage (rated 53 vs. 26 overall). For example, on average it takes 219
days to build a warehouse in Israel, compared to 70 days in the U.S. due to the licensing requirements.\textsuperscript{14} Perceived favoritism in government procurement processes (rated 47) is also problematic. Corporate taxes have historically been high, although recent changes should bring Israel in line with tax rates in the US and EU (target of 25% by 2010).

But perhaps the most important role the government has played is through activities of the Office of the Chief Scientist, which has incubated R&D, as well as the local capital market (see Exhibit 5). In 1993, the Office initiated Yozma, which successfully stimulated a local venture capital industry. Yozma was capitalized with $100M from the government, and split into 10 funds, each managed by an experienced foreign venture capitalist with a local partner. The parties were given the option to buy out the government’s 40% stake after five years; 8 of 10 funds did.\textsuperscript{15} Today, Israel’s venture industry trails only the U.S.’s, with more than $10 billion in capital raised.\textsuperscript{16}

**Exhibit 5: Cluster Development Activities through Office of the Chief Scientist**

<table>
<thead>
<tr>
<th>Activities Within Israel</th>
<th>International Activities (through MATIMOP)</th>
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<tr>
<td>R&amp;D Fund</td>
<td>Bi-National Funds</td>
</tr>
<tr>
<td>Supports industrial competitive R&amp;D projects; grants are on a sliding scale from 20%-50% of R&amp;D budget; royalty payment is 3%-5% of future product sales</td>
<td>Enable participation in a joint R&amp;D program with a foreign counterpart; grants are up to 50% of R&amp;D expenses of each company from each state</td>
</tr>
<tr>
<td>Technological Incubators</td>
<td>Bi-National Agreements</td>
</tr>
<tr>
<td>Provides a framework for nascent companies to develop their technology; program is open to private investors</td>
<td>Provide guidelines for granting support to joint R&amp;D projects.</td>
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<tr>
<td>Tnufa</td>
<td>EU Programs EP-6</td>
</tr>
<tr>
<td>The government and the investor will invest matching funds; the investor will be given an opportunity to purchase the government shares</td>
<td>Prime vehicle for Research &amp; Technological Development &amp; Demonstration (RTD) of the EU</td>
</tr>
<tr>
<td>Seed Fund (HEZNEK)</td>
<td>Eureka</td>
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<tr>
<td>Designed to encourage and support an individual entrepreneur; grants are up to 85% of approved expenses</td>
<td>Europe-wide network promoting collaborative market-driven R&amp;D projects</td>
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<td>Magnet (Magneton)</td>
<td>US-Israel Science &amp; Technology Commission</td>
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<tr>
<td>Promotes technology transfer from academic institutions to industry; grants are up to 60% of approved budget; no royalty payments</td>
<td>Launched in 1994, the Commission promotes bi-national cooperation at the highest levels of government and industry. Identifies and removes impediments and builds the infrastructure for mutually beneficial economic and technological cooperation</td>
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<td>Support for Research Institutes</td>
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2. CLUSTER ANALYSIS

The Israel biotechnology cluster has developed significantly over the past 20 years. The current challenge is to fully capitalize on a strong pool of basic research in order to transition from being internationally recognized to being internationally competitive in the early part of the value chain. In this section we provide an overview of the biotechnology industry, briefly chart the development of the biotechnology cluster in Israel, and analyze the cluster’s current position.

2.1. Overview of Biotechnology

Biotechnology may be broadly defined as “any technique that uses living organisms, or substances from those organisms, to make or modify a product, to improve plants or animals, or to develop microorganisms for specific uses.”\textsuperscript{17} The biotechnology industry therefore encompasses a very broad range of firms, fulfilling a diverse set of functions. Within the field of medical biotechnology, companies typically range from small start-ups, focused on developing basic research, to multi-billion dollar firms, such as Amgen or Genentech, that span the entire value chain from research and development to manufacturing and marketing.

The biotechnology industry shares many features with the pharmaceutical industry. Both industries are highly regulated and require significant capital to take products through the rigorous approval process and onto the market (see Exhibit 6). The average cost of developing a new prescription medication was estimated to be $987MM.\textsuperscript{18} For small biotechnology companies patents are critical in accessing capital and in establishing partnerships with larger firms. Partnerships are, however, important to all industry participants, combining the intellectual property of small firms with the expertise that larger, fully integrated, firms have in navigating the regulatory process and particularly in good manufacturing practices (GMP).
Manufacturing is particularly challenging for biotechnology as living cell cultures are required, and manufacturing facilities, of a scale necessary to fulfill market demand, can cost in the region of $600MM and take over 4 years to build.\textsuperscript{20} Moreover, the lengthy FDA approval process includes approval of the manufacturing process and site, so any subsequent attempts to move location or change process must be re-approved by the FDA.

For clusters, however, such requirements mean that once a plant is built it is unlikely to be moved. The key factor influencing a company’s decision to build a plant is not low labor costs, but a stable and permitting regulatory environment.\textsuperscript{21} Due to the magnitude of investment required and the uncertainty of the drug approval process, companies tend to delay the decision to build until the last possible moment. Once the decision is made to move forward, however, it is essential to build the plant as quickly as possible. The opportunity cost of a delay in manufacturing, and hence a delay in time to market, may become the dominant component of cost of a new plant. Thus, the potential for hold-ups due to local regulatory procedures, and lack of a standardized approval process, are major deterrents to companies to companies considering an area as a site for a facility.

Despite the many challenges of participating in biotechnology, the industry has, over the past decade, outperformed the NASDAQ, and consistently attracted high levels of venture capital and private investment – over $6.4B by some estimates, in 2004. Still, biotechnology is by its very nature a high risk, high reward industry; with only 1 in 250 compounds making it from preclinical development to market, many biotechnology companies will fail.
2.2. Worldwide Biotechnology Clusters

There are several prominent worldwide clusters in biotechnology, including clusters in Cambridge, Massachusetts, the San Francisco Bay Area, North Carolina, and Cambridge, UK.

By any measure, Massachusetts is the heart of the global biotechnology industry, generating 8% of the world’s pipeline of new medications. With several world-class universities spawning about 350 life sciences PhDs every year, the cluster has led to the formation of over 230 companies. Additionally, several of the world’s largest pharmaceutical companies – AstraZeneca, Abbott, Merck, and Pfizer – have chosen to locate their research and development facilities in the state.

Even in such an established cluster many challenges remain: increasing the rate at which research ideas are commercialized; maintaining position in an increasingly competitive biotech labor market; and facilitating companies’ moves down the value chain into manufacturing.

2.3. Development of the Biotechnology Cluster in Israel

The Israel biotechnology cluster has its roots in the research units of prominent Israeli universities. Over the past 20 years the cluster grown to over 150 companies and $2B revenues (see Exhibit 7) and has spawned many important drugs, including recombinant interferon-ß (Rebif) a drug widely used to treat Multiple Sclerosis.

*Exhibit 7: The Growth of the Biotechnology Cluster in Israel*
The millennium marked a turning point for the biotechnology cluster. With the publication of “Bioplan 2000-2010,” the latent potential of the biotechnology industry was recognized and its further development placed firmly on the national agenda. Through the Office of the Chief Scientist, a budget of $100MM was provided to establish two incubators dedicated to biotech, upgrade physical infrastructure, and provide pre-seed funding to support commercialization.

The Israel National Biotechnology Steering Committee was also established. Comprised of experts in biotech from industry and academia, the committee’s goals were to advise government on how to encourage business activities and investments in the industry, support the critical transition from academic research to commercialization, and facilitate international collaboration.

2.4. The Biotechnology Cluster in Israel Today

Today Israel’s biotechnology cluster is vibrant and growing. In this section we examine the cluster using the diamond framework (see Exhibit 8).

**Exhibit 8: Israel Biotechnology Cluster Diamond**

- Highly skilled workforce, esp. in advanced science and engineering
- High quality research institutes and structured collaborations between universities and industry
- Relatively high level of entrepreneurship — “aggressive, iconoclastic sensibility”
- Capital available particularly through the U.S. in the form of aid, as well as private venture capital and corporations investing in research and development activities but funding gap exists
- Lack of biotech managerial talent

**Factor (Input) Conditions**

**Context for Firm Strategy and Rivalry**

- Government support for entrepreneurial ventures through grants and incubators
- Fairly liberal regulatory regime (e.g. no restrictions on stem cell research)
- Regulatory standards are harmonized with the FDA
- Fairly easy access to US capital markets (e.g. NASDAQ)
- Overshadowed by high-tech as a government priority
- Lack of capital and liquidity on the Tel Aviv Stock Exchange

**Related and Supporting Industries**

- World leader in generic pharmaceuticals (Teva, an anchor pharmaceutical company in Israel) is starting to invest in biotech, but has led to IP protection being compromised
- Strength of high-tech sector may lead to a lack of management-inclined personnel in biotech sector

**Demand Conditions**

- Sophisticated hospitals and the highest number of doctors per capita in the world
- Significant ethnic homogeneity creates specialised demand for certain medical conditions (e.g. Tay Sachs, Gaucher disease both disproportionately affect people of Jewish origin)
- Relatively small market size (7.0MM) and low but growing per capita spending on medicines has led to export focus and higher product standards
2.4.1. Factor (Input) Conditions

Israel’s success in biotech is rooted in excellence in basic research and commercialization. A rich pool of talent resides in Israel’s universities and feeds the industry. In 2002, 22% of graduating doctoral students and 60% of scientific publications were in biological science.

Dedicated biotechnology departments are virtually unheard of anywhere, but three out of Israel’s seven main universities have them, and all universities have a commercialization agency which assists scientists in transitioning basic research into clinical products. The output has been impressive: Israel has the 4th highest number of biopharmaceutical patents per capita in the world.²⁴

Funding for research activities comes from both government and industry. Government funding is indirect, through the education budget, and direct, through programs such as MAGNET, which sponsors consortia of companies and universities to develop novel generic technologies, underwriting up to 65% of the budget. Industrial funding comes mainly from selling scientific expertise; in 2001, Hebrew University raised $12MM by this route.

While there is considerable support for scientists conducting biotechnology research, some have expressed concerns that recent education budget cuts will undermine further university research. Additionally, there is concern that the commercialization units do not offer enough assistance to scientists in protecting their intellectual property.

Despite the relative strength of the venture capital sector in Israel, the high risks involved in commercializing a biotechnology product makes attracting venture capital difficult, especially as the average size of VC fund is still significantly smaller in Israel than in the U.S. Furthermore, the large number of high-tech and medical device companies, which require less funding, makes it challenging for biotechnology firms to win VC investment (see Exhibit 9).

**Exhibit 9: VENTURE CAPITAL FOR BIOTECHNOLOGY IN ISRAEL**

- ~75 Israeli life-science companies raised $238 million in venture capital in 2000, up from $135 million in 1999²⁵
- Around 70 VC funds exist in Israel; over 25 have ‘significant healthcare investments.’ However **only ~5 funds are dedicated to biotechnology**, life science and medical equipment
- Seed investment in Israeli biotherapeutic companies averages between $2 and $3 million (compared to U.S. seed funding, which is typically between $10 and $15 million)²⁶
The strong demand and the limited supply of venture capital early in the drug development process creates a funding gap, particularly in the transition from discovery to pre-clinical phase, and then to Phase I. In many other countries, funding at this stage is available from different sources. For example, in the U.S., funding for early stage research and early-stage clinical trials is provided by the National Institute of Health.\textsuperscript{27} In Israel, the only dedicated biotechnology incubator – Bioline – has been established to provide funding up until the completion of the animal testing phase.

The shortage of venture capital funding is exacerbated by the lack of managerial talent for biotechnology companies. As the biotech companies in Israel are generally started by people from academia who often lack business experience, the concern around Israeli talent’s managerial ability to take a product to commercialization may deter to venture capital firms. The presence of only one large Israeli pharmaceutical company – a generic manufacturer with limited experience in commercializing early stage compounds – compounds this problem.\textsuperscript{28}

Recognizing the gaps in funding, infrastructure for early stage commercialization, and managerial talent, the Israeli Government set up incubators to bridge those gaps and help research coming out of universities along the path toward commercialization. There are currently 20 state run high-tech incubators,\textsuperscript{29} and approximately 25\% of companies within these incubators are biotechnology companies.\textsuperscript{30} Prior to 2000, none of the incubators focused on biotechnology, which has different requirements from the high-tech or even medical devices sectors. Bioplan 2000 outlined the creation of two dedicated biotechnology incubators. Bioline, initiated by the Government, is a consortium comprising private sector organizations (see Exhibit 10). The second dedicated incubator – to be run by the Hadassah Medical Organization and the Hebrew University of Jerusalem – is scheduled to be launched in 2007 in Jerusalem.

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\textbf{Exhibit 10: BIOLINE}\textsuperscript{31} \\
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Established: & 2004 \\
Location: & Jerusalem \\
Owners: & Teva Pharmaceuticals, Giza Venture Capital, Pitango Venture Capital, Hadasit \\
Scope: & Project focus vs. Company focus; Projects will be developed for up to three years, until the human experimental stage. Beyond this, the research will be transferred into a company (strategic partner), such as a pharmaceutical company. \\
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2.4.2. **Context for Firm Strategy and Rivalry**

**Industry Structure**

Biotechnology contributes 21% of the revenue of Israel’s life sciences cluster, which is currently dominated by the medical devices sub-sector (54% of revenue). There are numerous research and manufacturing activities within biotechnology; the key sub-sectors within biotechnology are drug discovery, genetics, and cell and tissue therapy (see Exhibit 11).

**Exhibit 11: Biotechnology Activity in Israel**

More than 90% of biotech companies in Israel are small enterprises of under 50 people – 66% have < 10 employees and about 50% of biotech employees work in small firms (see Exhibit 12).

**Exhibit 12: Overview of Israeli Biotech Sector by Firm Size and Investment Requirements**

Like other biotechnology clusters, particularly the Massachusetts and San Francisco clusters, most biotechnology companies in Israel are centered around the major universities. About 90% of
activities within the cluster take place within the triangle of Jerusalem, Tel Aviv and Haifa – all a two hour drive away from each other.

Although many biotechnology companies participate in various activities along the value chain, and are involved at different stages along the drug development funnel, most are involved in basic research (see Exhibit 13).

**Exhibit 13: Profiles of Selected Biotechnology Companies**

| Founded: | 2000 |
| Focus: | Agro-biotechnology; offering a novel solution for hybrid seed production to improve yield & quality |
| Products: | FertiSeeds – strawberry breeding program enabling off-season, early market cultivation |
| Dr. Shamay Etgar, CEO was a Professor of Genetics, Horticulture and Biotech, before founding the Center of Biotechnology |

| Focus: | Mid-1990s |
| Products: | Unique peptide-based drug targeting and delivery systems for unmet clinical needs |

| Focus: | Late 1990s |
| Products: | A drug targeting platform (S2DOT) – applications in cancer, cardiology, infectious diseases |
| Manufactures peptides and combinational compounds for laboratories in the pharmaceutical industry and academic institutions |
| Joined the Migal Incubator in 1999 |

| Focus: | 1989 |
| Products: | Infectious diseases, particularly Hepatitis B and C |

| Focus: | 1989 |
| Products: | HepaX-B – currently in Phase 1b trials, worldwide rights licensed to Cubist |
| XTL-6065 – currently in Phase 1 trials |
| XTL-2125 – expected to file for IND (Investigational new drug) application with the FDA in 2006 |
| Holds 23 patents, an additional 41 are pending |
| Listed on the London Stock Exchange in 2000 |

Despite the focus on early stage research, the track record for Israel biotechnology companies is strong: those that have made it to the commercialization stage and are publicly listed have done exceptionally well. The strong performance of Israel biotechnology companies is testament to their reputation for providing “excellent science.”
The reputation of world-class biotechnology research has led to some outsource of R&D in Israel, particularly by US companies. However, the process of scaling up biotechnology research and development to early, small-scale production (and beyond) requires asset-intensive infrastructure. One limitation of Israel’s biotechnology cluster is the lack of “established infrastructure for next-level companies, despite its considerable assets.”

Exhibit 14 shows the performance of the biotechnology and pharmaceutical indices of the Tel Aviv Stock Exchange (TASE). However, while this index has outperformed the overall market, it is clearly dominated by Teva’s performance, indicating that there is little biotech activity on TASE. There are two reasons for this: (1) The bulk of biotech activity in Israel focuses on early stage research, and commercialization is a rare occurrence; (2) Most Israel biotechnology companies that do go public IPO prefer listing on NASDAQ, as TASE is provides less liquidity.

**Regulatory Framework**

Israel has a very open scientific regulatory environment, and has become one of the leading countries in stem cell research. Israel is part of the international stem cell forum, and Israeli researchers were key players in the landmark isolation of stem cells from human embryos in 1998. This climate derives inspiration from Jewish teachings, which are orthodox in nature, but very liberal from a medical point of view. Healing and saving lives are of utmost priority in Judaic law. The justification to engage in stem cell research for therapeutic causes derives from this tradition.

While generally open and progressive, Israel has also been at the forefront of instituting regulations to specify what research is acceptable, which many other countries have not yet done. For example, Israel was one of the first countries to adopt legislation imposing a five-year moratorium on genetic intervention for the purpose of reproductive cloning (1998), a moratorium that in 2004 the Knesset extended until 2009. The 1998 Israeli law also prohibited germ-line gene therapy. The approach taken by the Israeli Parliament stems from the understanding that science in
this field is still in its infancy, so it is necessary to continuously assess the moral, legal, social and scientific connotations of the genetic interventions and their impact on human dignity.

Israel is currently forming a national council of bioethics, which will serve as a governmental statutory authority. Its responsibilities will include monitoring of existing committees and advising the Knesset, Government and courts on ethical questions arising from biotechnological research, medicine and genetics. It will also be responsible for engaging the public in bioethical questions and for representing Israel in international bioethics forums.

Within Israel, drug regulation is overseen by the Institute of Examination and Regulation, a department of the Israeli Ministry of Health. Recent announcements that the Ministry of Finance is attempting to privatize this department have been greeted with dismay by the health ministry and resulted in a slow-down in the drugs approvals process in recent months.41

The Israeli Ministry of Health has successfully harmonized relations with the U.S. Food and Drug Administration (FDA) to enable full acceptance and recognition by the FDA of clinical trials conducted in Israel for registration of new drugs and medical devices.42 Under the auspices of U.S.-Israel Science and Technology Foundation, the FDA is working with the Israeli Health Ministry to adopt American standards for testing drugs and medical devices so that these tests can be accepted by the FDA, and to facilitate joint trials of drugs and devices by American and Israeli companies. A proposed joint trial with America’s Silicon Graphics, Ltd. and Israel’s Diasonics Ltd. to test a diagnostic ultrasound system would be the first of its kind between the U.S. and a foreign country of a medical device. The two countries also hope to reach an intergovernmental agreement accepting local inspections of facilities and plants that produce drugs and/or medical devices, and formalizing local monitoring in either country. A common set of standards will given US companies greater access to Israel's pharmaceutical and medical technology, encourage US-Israeli partnerships and eliminate duplicate testing of Israeli-approved products in the US. It will also allow researchers to conduct more clinical trials in Israel, taking advantage of the country's concentrated population and highly-skilled scientific community, making tests more cost effective and easier to monitor.43
2.4.3 Related and Supporting Industries

As touched on briefly in the section on context for firm strategy and rivalry (2.4.2), the Israeli biotechnology sector is part of a young and growing life sciences cluster that includes the medical device and pharmaceutical sectors. Of the 557 companies currently listed in Israeli Life Sciences Institute database, 45% were established in the last five years, and 77% during the last decade.

Consequently, many Israeli life sciences companies are in the early development stage and 63% are not yet revenue producing (see Exhibit 15). This large number of entrepreneurial companies has attracted significant numbers of supporting firms – such as lawyers and accountants, who are well positioned to advise small, entrepreneurial ventures.

Exhibit 15: Number of Companies and Developmental Stage

![Exhibit 15: Number of Companies and Developmental Stage](image)

Although the medical device sector has the largest number of firms, the pharmaceutical sector is by far the most established and the largest in terms of revenue.\(^4^4\) Leading Israeli pharmaceutical companies, such as Teva (established as far back as 1901), Agis, Taro and Dexcel, are focused on generic drugs, although all of these firms are also involved in the development of new drugs (known in the field as “new chemical entities”). Other Israeli firms are involved in the development of drug delivery and vaccines, while some develop new drugs using natural compounds.

Teva is an anchor company for Israel in the life sciences space, and has become one of the world’s largest generic pharmaceutical companies in the world, with more than 13,000 employees.

\(^{44}\) Source: ILSI Database; * 2005 to date at time of survey
worldwide and production facilities in Israel, North America, Europe and Mexico. The company is involved in the development, manufacturing and marketing of generic and innovative human pharmaceuticals and active pharmaceutical ingredients. In 2003, Teva earned $1.3 billion in net income off $5.3 billion in sales, almost 90% of which was in North America and Europe.

While the strength of the life sciences cluster in general is positive for the international reputation of Israeli biotech companies, the strength of the generic pharmaceutical companies has led to unusual intellectual property (IP) laws. In general, Israeli IP laws conform to international standards, with drugs given marketing exclusivity rights similar to those found in the US and Western Europe. However, data exclusivity standards are different. In most developed economies, drug companies applying for a new drug must present national regulatory authorities with comprehensive data showing the drug’s safety and efficacy profile and evidence from clinical studies. This data is normally regarded by the regulatory authority as confidential. In Israel
however, patent law was amended in 2005 to allow Israeli companies to access these regulatory filings. This law has been labeled by the media as the “Teva Amendment,” because it is designed to benefit Teva and Israel’s other generic pharmaceutical manufacturers, who can use this data to prepare their own competing products so they are ready as soon as marketing exclusivity rights come to an end.

This exemption has met with criticism and concern among multinational pharma companies and other pharma patent holders, and has been a topic of debate on the diplomatic level between Israel and the U.S. In April 2005, the U.S. announced that it would put Israel on its “priority watch list” of countries that violate IP rights. The United States also voiced concerns about the continuing problems experienced by U.S. firms, claiming that they suffer from a lack of adequate protection for their intellectual property in Israel due to an onerous patent system that allows competitors to delay the granting of patent rights through open-ended, pre-grant opposition proceedings, as well as weak protection of proprietary data against unfair commercial use.45
2.4.4 Local Demand

Israel has a small, but sophisticated healthcare market. The country has number of world-class hospitals, a high level of total health expenditure as a percent of GDP compared to other developed countries, and one of the highest number of physicians per capita in the world (see Exhibit 17).

Exhibit 17: Spending on Health and Number of Physicians Per Capita

![Graph showing National Expenditure on Health (% of GDP) and Rate of Physicians per 1000 People across various countries.](source)

However, Israel’s spending on medicines as a percent of GDP, lags behind other developed economies, even though it has grown in recent years (see Exhibit 18). In 2002, Israel had the lowest total per capita spending on medicines ($197 PPP) of all OECD countries. There are a number of reasons to explain this. First, Israel’s population is relatively young compared to most other developed economies, so medication use is lower. Second, actual prices of medicines are low, a result of the growing impact of National Health Insurance (NHI) budgetary pressures on HMOs as well as increases in prescription sharing by patients. The impact is felt both on the demand side (higher co-payments, administrative and prescribing restrictions) and on the supply side (price competition, mainly from generics). Substantial extra funding for the addition of new drugs to the NHI basket in recent years has had no overall impact on longer-term spending patterns.46
2.4.5 Institutes for Collaboration

Two IfCs represent the interests of the Israeli biotech cluster: the Israel Life Science Industry (ILSI) and the Israel Biotechnology Organization (IBO) (see Exhibit 19). The ILSI is the larger organization and represents a wider range of life science sectors, including medical devices and pharmaceuticals, while the IBO is solely focused on biotechnology. Neither organization appears to be particularly prominent or active – indeed, given the tension between generic pharmaceutical manufacturers and biotech firms, ILSI may find itself in a paralyzing situation.

Exhibit 19: Israeli Institutes for Collaboration

| Mission: | To research, develop and advocate policies and actions that promote medical devices, biotechnology, pharmaceutical and agricultural-biotech in the State of Israel and increase awareness of its strength and innovation worldwide |
| Number of Members: | ~300 companies |
| Objectives: | • Enhance interaction and provide a unified voice for its members  
• Disseminate scientific information to and provide opportunities for networking between companies, potential investors and other parties  
• Provide forums for the academic community and the health technology industry, to foster innovation  
• Provide a forum to identify, analyze and develop positions on public policy issues that affect Israel’s biomedical and health care technology interests |

Israel Biotechnology Organization

To promote biotechnology industries in Israel and to create a supportive environment for their growth. The IBO places special emphasis on dealing with “start-up” companies and entrepreneurs, some not yet members of the organization.

~50 companies

• Marketing the Israeli biotechnology industry among investors, as well as local and foreign clients. The IBO participates in exhibitions, conference and seminars held in Israel and abroad.

• Activities vis-à-vis government ministries, for the purpose of increasing investments and stabilizing biotechnology industries in Israel.

• Disseminating information and creating business ties – the IBO initiates and organizes study days and conferences
3. ISSUES AND RECOMMENDATIONS

3.1 Country Issues

Since Israel’s foundation in 1948, its economy has been shaped by the ongoing conflict with its Arab neighbors. Indeed, today regional instability remains the largest threat to the Israeli economy. Nevertheless, much remains to be done internally to overcome the legacy of decades of socialist policies and become even more globally competitive. In the following section, we outline the economic, political and social challenges facing Israel.

Economic Challenges

Recent economic reforms have helped Israel become a business environment that enables innovative local businesses and attracts foreign investment. However, much remains to be done to remove barriers, improve financial and human capital markets, and reduce dependence on the U.S.

- A significant amount of bureaucratic red tape remains the country’s greatest competitive disadvantage, with complicated government processes, a lack of transparency, and perceived government favoritism in procurement.
- The corporate tax rate is still high and some trade barriers exist, affecting about 15% of imports, particularly agricultural products and some products from East Asia.
- The Tel Aviv Stock Exchange remains underdeveloped and offers a poor exit strategy.
- Israel lacks a depth of experienced, native managerial talent. Although the country has attracted some foreign talent, in part as members of the Jewish diaspora go to Israel to make aliyah, perceptions about the security situation may make it less attractive to Westerners.
- Israel may gradually need to reduce dependence on U.S. aid. Although the total amount of aid is expected to remain roughly flat, it is shifting away from economic aid (currently ~$1B) and toward military aid (currently ~$2B), with the intent of phasing out the economic component. If
reductions in economic aid force decreases in the education budget – a key source of funds for basic science research in Israel – this may pose a risk to the quality of scientific research.

**Social and Political Challenges**

Israel faces challenges around social inequities and immigration, as well as economic reform.

- Although the **unemployment** rate has dropped over the past two years, it remains relatively high at 8.9%. In part, this reflects challenges in integrating the almost 100,000 immigrants from North Africa, particularly Ethiopia. As the economy has transitioned toward a knowledge economy, it has become increasingly difficult to integrate lower-skilled workers, particularly given **discrimination** toward these newer immigrants as well as toward Arab Israelis. These troubling **social inequities** exacerbate an already volatile environment.

- The public has had a mixed response to **recent economic reforms**, which included a slew of budget cuts affecting welfare payments, education and the health service. Even though the power of the labor federation, Histadrut, is not what it once was, it may be challenging to withstand political pressures to slow, or even, reverse unpopular reforms, particularly given the potential need make concessions to secure political coalitions.

**3.2 Country Recommendation**

Clearly the shadow of conflict with neighboring countries still represents the greatest threat to Israel’s economic future, and finding a path toward peace will be an essential priority. But beyond this obvious focus, there are other, easier to implement steps to help improve Israel’s development.
Government

- Where possible, consider promoting increased regional trade as means to peace and improving the wealth of the neighborhood.

- Reduce the legacy of bureaucratic red tape by simplifying the number of steps required in administrative and regulatory processes. Revamp government decision-making processes, particularly procurement, to increase transparency, changing the culture of what is tolerated through a few quick, highly visible changes.

- Continue to reduce the few remaining trade barriers and taxes. Continue privatization to around infrastructure (e.g. ports).

- Encourage local capital market development to upgrade sophistication of financial system, and create local exit opportunities, potentially taking advantage of U.S. connections.

- Provide incentives to deepen native executive talent by seeking to attract and develop larger companies with deep management benches. Invest in business schools and create rotational programs so professionals can gain exposure to management in more advanced countries before returning to Israel. Encourage the return of ex-pats, members of the Jewish diaspora, as well as those without a cultural tie to the state.

- Improve the country’s public image by marketing its economic assets to attract FDI and offset, even somewhat, negative publicity about security issues.

- Ensure equal opportunities for immigrants and Arab-Israelis through education and social advancement, and increased awareness of the problem of discrimination.

Firms / Institutions for Collaboration

- Help upgrade executive talent by developing local and rotational training programs both at business schools and at firms, and improving recruitment of foreign talent.
3.3 Cluster Issues

In further developing the biotech cluster a number of issues need to be addressed.

- With the exception of basic research there is a general **lack of expertise in development, manufacturing and marketing of products** which poses a major restriction on the commercialization of basic research. Due to the expense associated with developing a manufacturing facility, it is unlikely that any firm will develop these capabilities soon.

- Israeli biotech firms face considerable **difficulty in gaining access to capital**. Education budget cuts are affecting basic research and there is limited capital available to transition basic research to the point of being considered for VC funding. While incubators have the ability to address this problem, there are still very few dedicated biotech incubators.

- While the biotech cluster draws from a deep pool of scientific talent it **lacks equally developed managerial talent**. Such managerial expertise is essential in the development stage and in realizing the value of products on the world market.

- **Inadequate protection of intellectual property remains a significant problem** which inhibits collaboration between Israeli biotech firms and external firms and may also hinder foreign direct investment in the biotech cluster.

- The existing **Institutes for Collaboration are ineffective** in fulfilling the needs of the biotech cluster. The largest (ISLI) represents the entire life sciences cluster and the only biotechnology dedicated IFC (IBO) is small is doing little to address the challenges the cluster is facing.

- The **biotech cluster does not adequately leverage the wider life sciences and high tech clusters**. While biotech firms do co-exist in incubators with high tech and medical device firms there is little interaction between different industries; the networks underpinning the biotechnology cluster are predominately university related, while those in the high-tech and medical device sectors derive from military service. At the interface of these different industries lies a significant opportunity which is currently unrealized.
• For all the government rhetoric surrounding the biotech cluster the **government has been slow to act on its promises.** Of the two dedicated biotech incubators promised in Bioplan 2000-2010 only one has been built and the other is scheduled for completion in 2007.

### 3.4 Cluster Recommendations

The cluster should focus on developing its capabilities in product development – gaining the experience and expertise of conducting clinical trials and working with regulatory authorities. This will require greater numbers of professional managers and more capital. The government, IFCs and firms each have a role to play.

**Government**

The government, in consultation with the Israel National Biotechnology Steering Committee, should:

- Encourage the development of **courses at local business schools focused on the life-sciences management** and promote biotech an attractive place to work, even for people without a life-sciences background

- **Establish work placement programs** with world-leading biotechnology companies, particularly in biotechnology hubs (e.g. Massachusetts and California)

- **Accelerate the building of the second bio-tech focused incubator**, currently due to come online in 2007, and consider establishing additional incubators. Such facilities allow new firms to focus on developing products not building facilities

- Provide capital to continue to fund basic research in universities (through the education budget) and to offer grants to assist firms in bridging the funding gap.

- Overturn the “Teva amendment”, such that **Israeli IP conforms to international standards** in data exclusivity as well as market exclusivity.
• **Create the position of “Development Officer”** within the Office of the Chief Scientist and recruit an individual with extensive, private sector, drug development expertise. As a general resource to Israeli biotech firms, this office would provide advice and assistance on drug development, clinical trials and navigating the regulatory process*

• Promote Israel as an **attractive destination for world-class life-sciences firms**. The Government should actively court leading pharmaceutical and biotechnology companies to develop a research facility in Israel, citing the excellence of local scientists, the open science environment and the alignment with US regulatory requirements.

**Institutes for Collaboration**

The Israel Biotechnology Organization (IBO) should play a more active role in influencing government policy and facilitating information exchange among firms. In particular, they should:

• **Lobby the government** to repeal the Teva Amendment.

• **Facilitate forums for biotech firms to meet potential partners**, including VC firms and other capital providers, and bio-pharmaceutical firms with manufacturing and marketing capabilities.

• **Lead education seminars** on drug development, and on recent developments in the life sciences and high tech sectors.

**Firms**

As they look to progress beyond basic research, firms should:

• **Acknowledge the role of professional managers** as complements to the scientific expertise of the founders.

• **Be more demanding of the IBO**, and take greater leadership roles in this organization.

* To prevent conflicts of interest, the Office of the Chief Scientist should have no say in regulatory decisions, as is currently the case
Endnotes

1 Jewellery and precious metals, includes only net exports of polished diamonds to reflect value-added activities (exclusive of raw materials). This is roughly one-quarter of the total value of diamond exports, including raw materials.

2 Men serve for three years as do women in combat positions; women in non-combat positions serve for two years.

3 http://hcs.harvard.edu/~hireview/content.php?type=article&issue=spring04/&name=feith


6 Based on 2004 data. Rated 22 on National Business Competitiveness Ranking 2005

7 Global Competitiveness Report 2005


12 The national airline El Al was finally privatized in 2003, the Israel Discount bank and telecom provider Bezeq in 2005, while the port system has been separated into four SOEs still pending for privatization.


14 The World Bank http://www.doingbusiness.org/ExploreTopics/DealingWithLicenses/


16 Israel Venture Association, http://www.iva.co.il/content.asp?pageId=36

17 Tufts Center for the Study of Drug Development


19 Global Competitiveness Report, 2005


23 The Yozma Group, “Early Stage Investments: The Israeli Perspective,” http://www3.usal.es/~paxisworkshop/477,1


25 The Israel National Biotechnology Steering Committee http://www.irc.org.il/biotech/INBSC.htm


32 ILSI database, 2005.

33 ILSI database, 2005.

34 ILSI database, 2005.


40 Science Magazine, March, 2002. This section draws from Adee Matan, Israel Science Report, British Embassy Tel Aviv, December 2004

People we have spoken to during the course of our research

- Haim Aviv, CEO of Pharmos, Corp., “father of Israeli biotechnology” founder Biotechnology General Inc. as well as Novamed Ltd., Peptor Ltd., and HerbaMed Ltd.
- Ruti Avon, Managing Director of Healthcare Ventures, Pitando Venture capital, Israel
- Dan Isenberg, Senior Lecturer, Harvard Business School (20+ years VC experience in Israel)
- Isaac Kohlberg, Senior Associate Provost, Chief Technology Development Officer, Harvard University
- Neil Cohen, General Partner of Israel Seed Partners, a leading Israeli venture capital firm, co-founded in 1995, head of the life sciences practice
- Sho Matsubara, MOC alumnus
- Alex Rogers, MOC alumnus, HarbourVest Partners (U.K.) Limited
- Pascal Rosenfeld, CFO of ETC-VISION, a high-tech company dedicated to smart video surveillance, Paris, France
- Jonathan Solomon, Harvard Business School MBA candidate
- Beka Solomon, Professor, Department of Molecular Microbiology and Biotechnology at the George S. Wise Faculty of Life Sciences at Tel Aviv University
- Didier Toubia, MSc, MBA, Chairman of Biomed Israel