



DIGITAL HEALTH: THE ISRAELI PROMISE

JANUARY 2020

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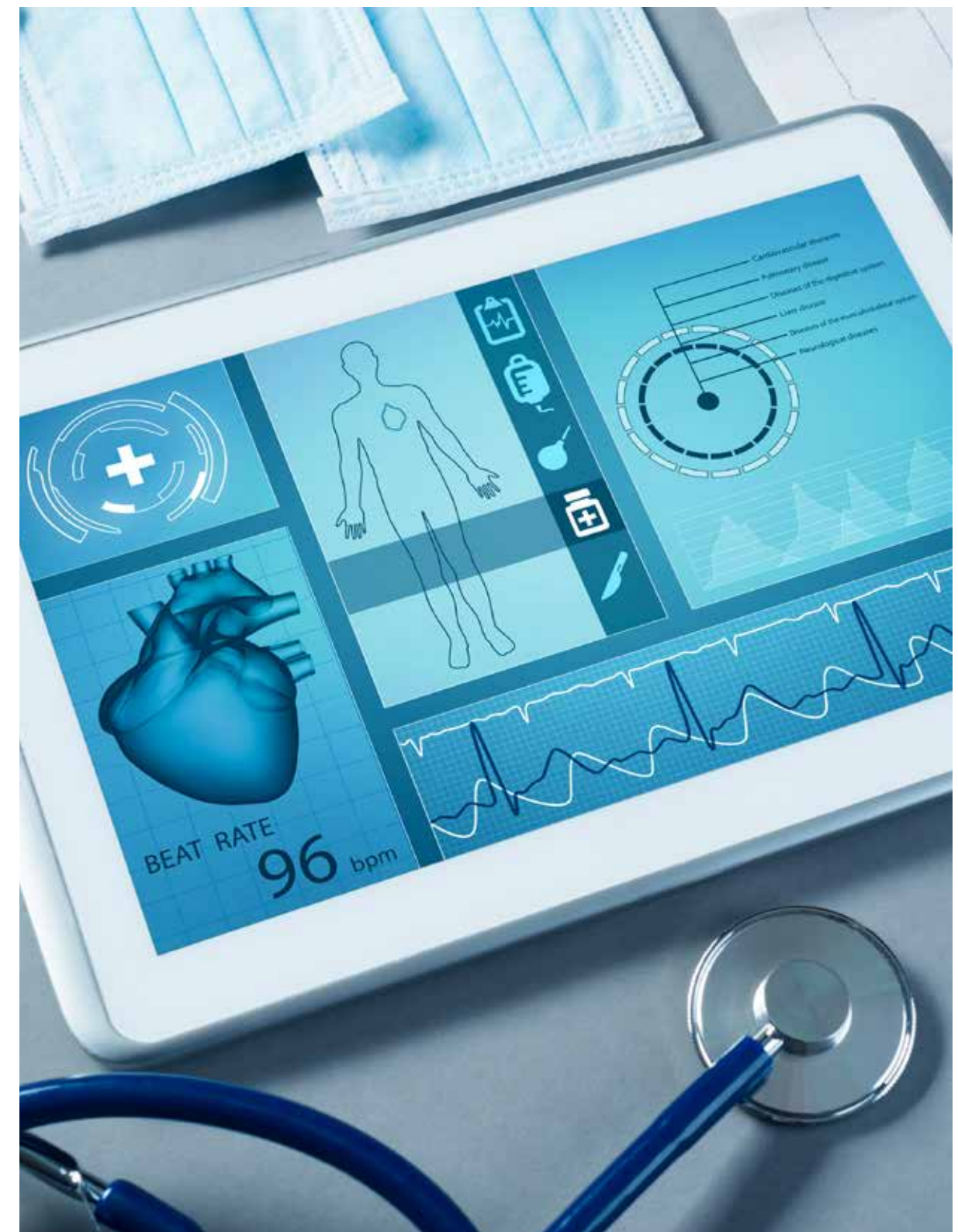
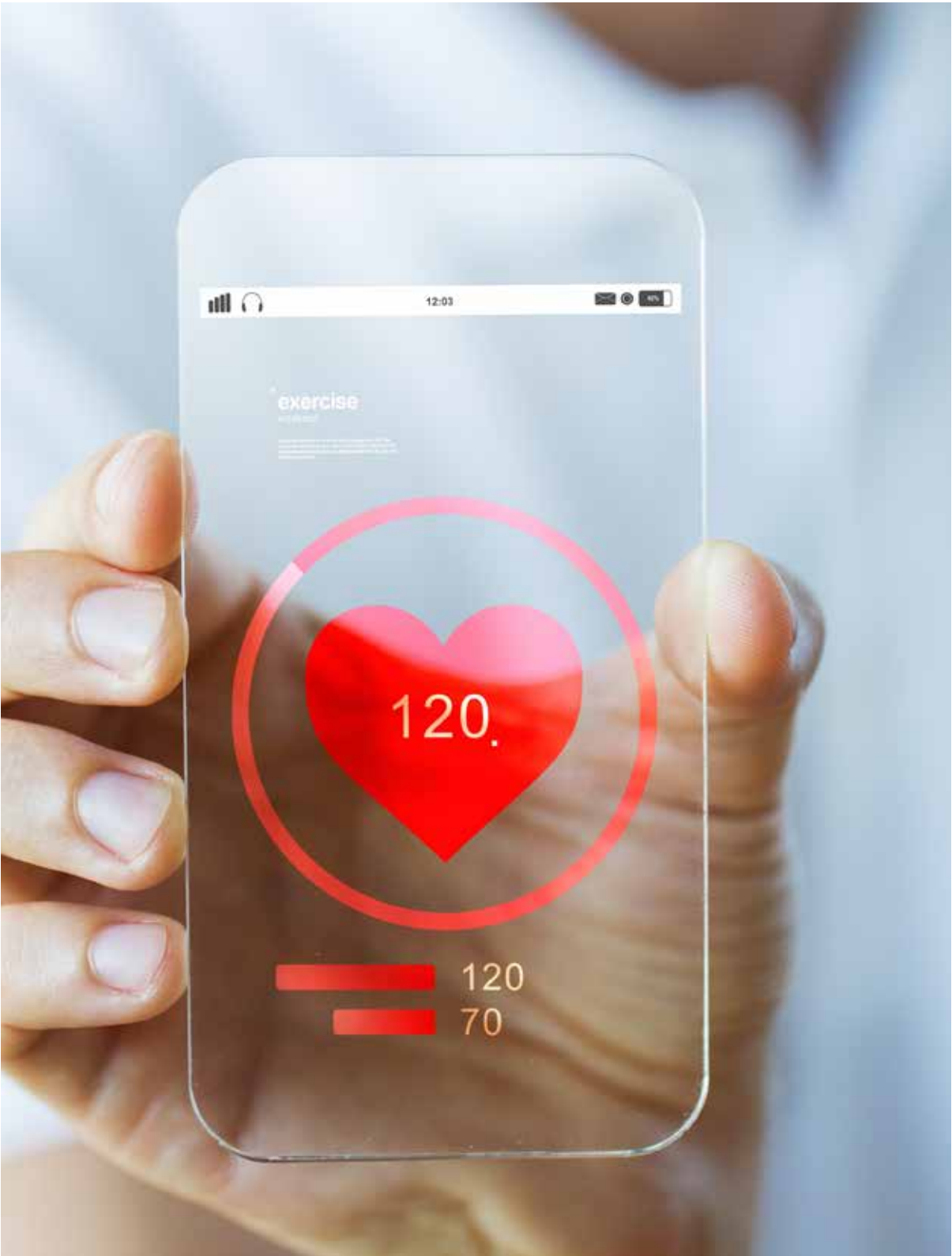


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EXECUTIVE SUMMARY

The digital health sector is one of the most promising areas in terms of global growth, and is expected to grow significantly by 2024, reaching a market size of over \$200 billion globally.

Israel seems to be a major player in this ecosystem: its share of investment has grown significantly between 2014 to 2019, from 1.5% of global investments in digital health to 4.5%, while the country's population represents about 0.1% of the global population.

There is a wide range of both traditional and non-traditional players aiming to penetrate the market, each with its own unique strategic goals, R&D, deployment strategies and channels to the healthcare market. One thing is common to all - they're all looking for the next big thing in digital health, and seek to incorporate innovation in the most impactful and efficient way.

Israel's digital ecosystem offers a fertile ground for a wide variety of players with substantially different needs to develop their digital health open innovation strategy.

The ecosystem has several key components:

- Over 550 active digital health start-ups from a wide variety of digital health segments, half of them at post-product phase

- High-quality, community based healthcare system, which offers a unique set of 25 years-old digital databases, as well as beta sites and innovation hubs

- Mature medical device, pharma and tech industries with global business know-how

- Advanced AI, cyber-security and additional computer sciences and life science skills

- Extensive support from VCs, associations, NGO's and the government

These components combined offer global players a relatively low risk – high reward environment, through access to a high-quality innovation deal flow and fast, cost effective R&D and clinical trials validation cycles. Many market leaders have already established a significant presence in Israel, among them: Medtronic, Philips, GE Healthcare & Change Healthcare, as described in the case studies section at the end of the paper.

We hope this paper will shed light on Israel's 'digital health promise', and help global players eying the field to understand their opportunities and to establish and grow their presence in Israel.



1. THE GLOBAL DIGITAL HEALTH MARKET & ISRAEL'S POSITION

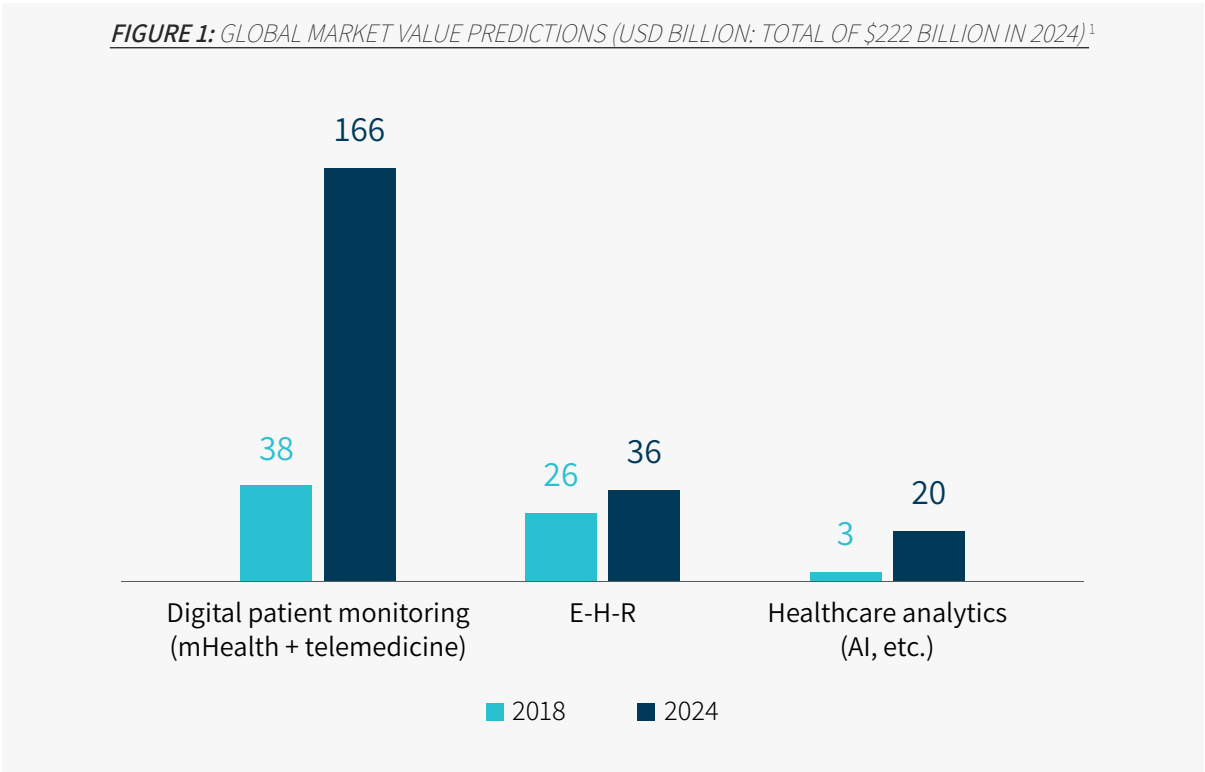
Market Growth and Investment Trends

The global digital health market is experiencing substantial growth, and is expected to keep growing at a double digit growth rate, reaching \$200 billion by 2022.

The market is traditionally divided into four main categories:

- 1. Telemedicine:** The use of telecommunication and information technology to provide remote healthcare services, including consulting, treatment, surgery and education.
- 2. mHealth:** The use of mobile phones and other wireless technologies (sensors, IoT, wearables, etc.) in medical care, the most common application of which is using mobile devices to educate consumers and collect data.

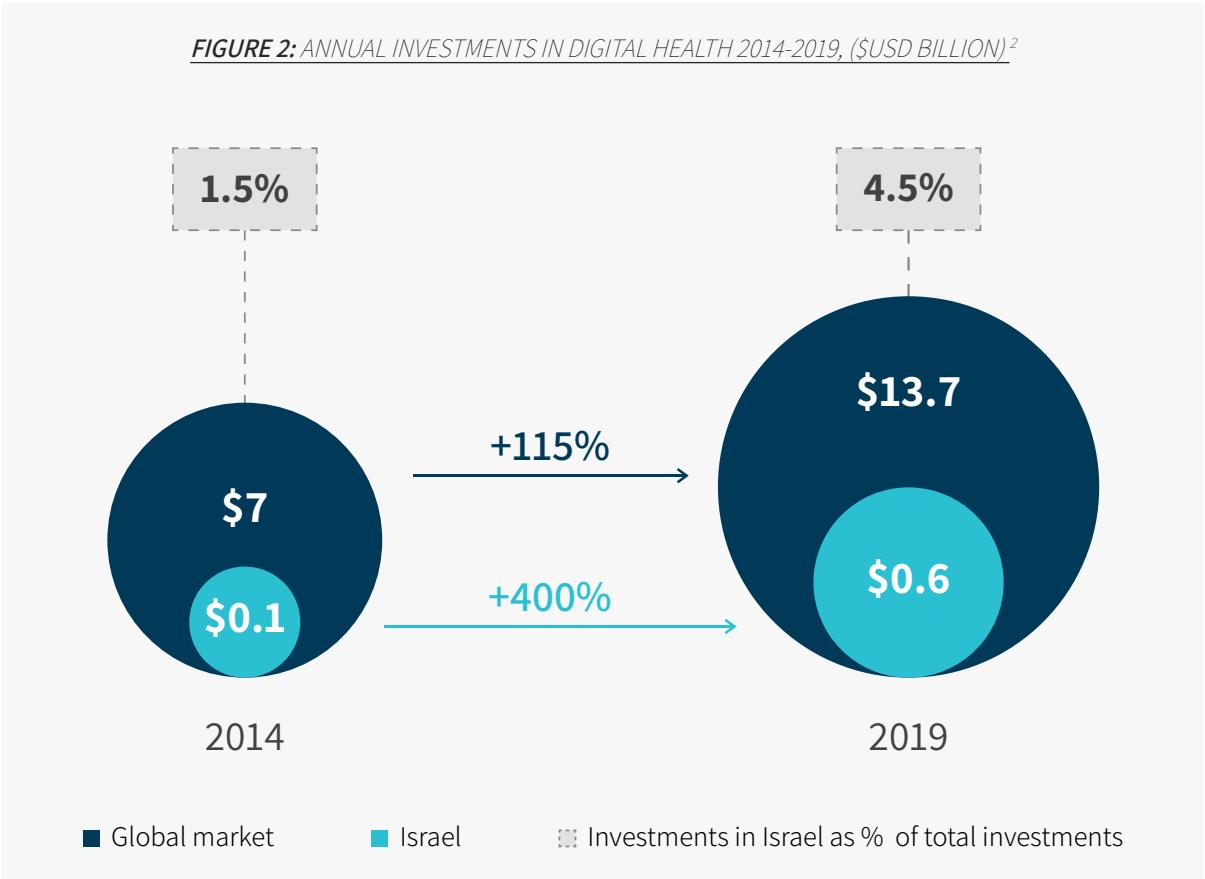
- 3. Electronic medical records (EMRs) & healthcare IT:** EMRs are IT systems which are used to collect, store and manage patient health information in a digital format. Those systems may connect to various IT applications, including: health administration & supply chain management, billing automation, documents and image management, e-prescriptions, and more.
- 4. Health analytics, cognitive computing and artificial intelligence:** Improving healthcare services, research and development based on insights from patterns and correlations found in health related big data (from EMRs, genetic sequencing, etc.), using cognitive computing and artificial intelligence technologies and applications.



While the EHR market is relatively stagnant, Digital patient monitoring (Telemedicine+mHealth) and Health Analytics segments are expected to enjoy the most significant growth; Total market size is expected to reach over \$200 billion in 2024.

1. THE GLOBAL DIGITAL HEALTH MARKET & ISRAEL'S POSITION

Accordingly, investments in digital health are on the rise. Global investment in digital health grew by 20% CAGR between 2014 to 2019, and reached \$14 billion in 2019. Alongside global growth, Israel has been attracting a significant share of these investments, doubling its share of global investments, growing from 1.5% in 2014 to 4.5% in 2019, representing 40% compound annual growth rate.



A growing number of market leaders also identify Israel as one of the most prominent digital health hubs, and its assets receive global acknowledgement and traction. These are manifested through enhanced activities, re-occurring visits, and increasing cooperation with local leaders by multi-national players.



In this paper, we review global players' motivations and strategies to enhance their digital health abilities, and describe ways in which the Israeli ecosystem meets their innovation needs.

2. GLOBAL PLAYERS' DIGITAL HEALTH PRIORITIES

The digital health market is attracting a wide variety of players from various market segments, both traditional healthcare players, as well as players with little or no connection to the field.

There are several reasons explaining the surge of new entrants to the digital health market: first, the digital health market is based on the convergence of digital technologies with health, and offers opportunities for software, hardware, cyber security and telecom infrastructure players, among others. Second, the ongoing transformations in the way healthcare services are being consumed and patients' preferences, have driven both insurance, as well as retail and logistics companies closer to the healthcare sector.

In the following chapter, we review the digital health priorities and motivations of different companies by industry sector.

MEDICAL DEVICE COMPANIES

An analysis of leading medical device companies, as well as in depth interviews,³ shows several digital health priorities they have in common. Market leaders use digital health solutions to improve their internal operations (e.g. to assist in real time decision making), design better equipment, individualize patient care and improve patients and clinicians' experience using their device.

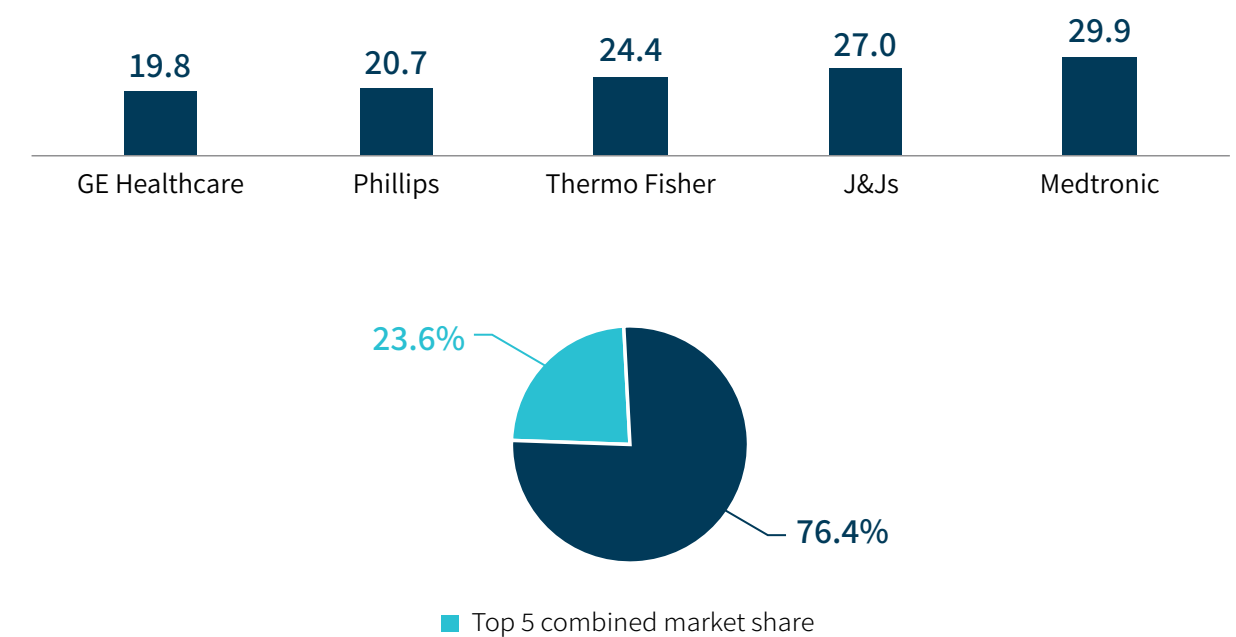
To achieve their goals, market leaders are engaging in acquisitions and in partnerships with other leading corporates. Acquisitions in digital health

tend to be of relatively small scale compared to their acquisitions in their traditional markets, which may imply that digital health is still in a growth stage. In addition, many of the leaders engage with the start-up ecosystem in other ways. Most of them own VC funds, or invest in a local VC fund which helps them identify and gain access to a high quality deal flow. They may invest in additional activities, for example, Boston Scientific has launched an open innovation model – the 'annual connected patient' challenge, a global contest aimed for companies and individuals to turn big data into actionable intelligence.

Based on our review of key opinion leaders (e.g., JP Morgan's investment review in MIXiii-BIOMED 2019), it seems that the medical device companies are somewhat more prone to invest in digital health, compared to pharmaceuticals for example, as their core activities and operation models are closer to the digital health models, rather than pharma. However, in both cases market leaders are engaging in the digital health industry through VC funding, accelerators and small scale acquisitions.

MARKET LEADERS' KEY MOVES IN DIGITAL HEALTH

FIGURE 4: TOP 5 MEDICAL DEVICE COMPANIES GLOBAL REVENUES (\$USD BILLION) AND SHARE OF GLOBAL MARKET (%), 2018⁴



Medtronic

Medtronic has been investing heavily in its digital health offering in recent years. Its notable activities include the acquisition of AI-powered nutrition platform, Nutrino Health in November 2018, for approximately \$100 million and peel-and-stick wearable heart monitor company Corventis in 2015 for a similar amount. In addition, in 2015, Medtronic announced a strategic alliance with Samsung Electronics America, a global leader in consumer

electronics and digital health, to accelerate the development of digital health solutions for various chronic conditions and neuromodulation therapies (Including movement disorders, chronic pain, etc.).⁵ Furthermore, Medtronic's integrated health care solutions unit aims to improve operational excellence in hospitals and clinics, through the application of analytics in end-to-end operations.

2. GLOBAL PLAYERS' DIGITAL HEALTH PRIORITIES

ThermoFisher SCIENTIFIC

Thermo Fisher manages its digital health business mostly through two brands. The thermo scientific brand's product portfolio includes innovative technologies and software for informatics, therapeutic drug monitoring testing and environmental monitoring and process control. The Applied Biosystems brand offers genetic analysis software for clients in research, clinical and applied markets. These include technologies for genetic sequencing that are used to determine meaningful genetic information in applications such as cancer diagnostics and inherited and infectious disease. The company's latest notable acquisition was BD's Advanced Bioprocessing, expanding its bioproduction offering to its clients with technologies for improved environmental and process monitoring and consumer safety.⁶



Royal Philips's emerging connected care & health informatics business started operating as an integrated business unit in 2018 aiming to digitize diagnostics in anatomic pathology, and to use artificial intelligence in disease detection and progression monitoring, reducing variability and improving outcomes.

The business is divided into four main parts,

monitoring & analytics, therapeutic care, health care informatics and population health management.⁷

Additional notable acquisitions in the past few years include the therapeutics division acquisition of UK-based Remote Diagnostics Technologies (RDT Ltd.) which provides pre-hospital monitoring and data management. The informatics division is highly focused on artificial intelligence at the point of care, and mentioned in Philips 2018 Annual Report, proof of clinical and economic outcomes, connectivity and cyber security are its key priorities. For example, the company acquired interoperability software solutions provider, Forcare. The population health management unit is focused on management of chronic conditions, including actionable programs to reduce risk, and offers cloud based solutions for organizations. The unit has recently acquired 'Well-incentive', 'VitalHealth' and 'Blue Willow' systems to enrich its offerings to organizations.



GE Healthcare

GE Healthcare provides a wide range of applications and platforms as part of its digital portfolio, including enterprise, workflow and financial management, diagnostic and monitoring solutions, drug development and an extensive health cloud services platform. The company also offers tele-training solutions (remote training) for radiology training, and offers a wide range of patient monitoring solutions. Overall, GE's vast offering serves as fertile grounds for new technology to be incorporated within GE's solutions. In terms of digital health strategy, the

company seems to be less focused on acquisitions, other than the acquisition of UK-based Monica Healthcare in 2017. In this case, the company had a long term relationship and served as GE's distributor prior to the acquisition. In addition to acquisition activity, the company seems to prefer strategic partnerships, for example, its JV with Roche, which aims to build a joint acute care decision system, or the recent partnership with Intel to develop a new AI imaging solution to accelerate critical patient diagnosis.⁸

PHARMA & LIFE SCIENCES COMPANIES

Pharma companies are also active in the digital health world. They use digital health solutions to improve their operation and development abilities, mainly shortening R&D cycles from discovery to launch, as well as seeking new targets and markets. Precision medicine is also on the rise, and requires the use of multiple data sources (genetics, patient health records, etc.), advanced mathematical models, and computation skills, also known as 'computational biology skills' (for example, DNA sequencing using big data).

An additional priority area is revolutionizing clinical trials using mHealth and data analytics tools, in order to refine candidates' choice, attract more patients and help them engage easily in clinical trials using remote devices. Lastly, launching complementary products, a trend known as 'going beyond the pill', is highly dominant among pharma giants which are expanding their drug offering to include apps

for disease management, patient monitoring and improved medical adherence.

Similarly to medical device leaders, pharma companies engage in digital health by acquiring small, innovative companies in the AI & mHealth fields, although there were several more significant acquisitions in the EMR / Healthcare IT – the more mature segments of digital health.

They also hold events and competitions for innovative companies (for example, J&J & Humana's challenge), led by their innovation units (for example, J&J's JLABS incubator), in order to seek new opportunities for the companies' various business units.

Other than engaging in external innovation, the companies are developing their own solutions in the digital health field, and aim to use available resources such as vast databases, which include genomics and clinical health records, among others, combined with advanced analytical and machine learning tools. They often prefer to operate in hubs, which foster open innovation, and have academic institutions, medical device, start-ups and healthcare providers, as well as wide access to datasets, all in an adjacent geographic location.

An interview with a business development manager from one of the largest multi-national pharma companies highlights their key needs when choosing where to locate their digital health R&D:

"What our company needs is a 'sandbox': connected and open databases which include

2. GLOBAL PLAYERS' DIGITAL HEALTH PRIORITIES

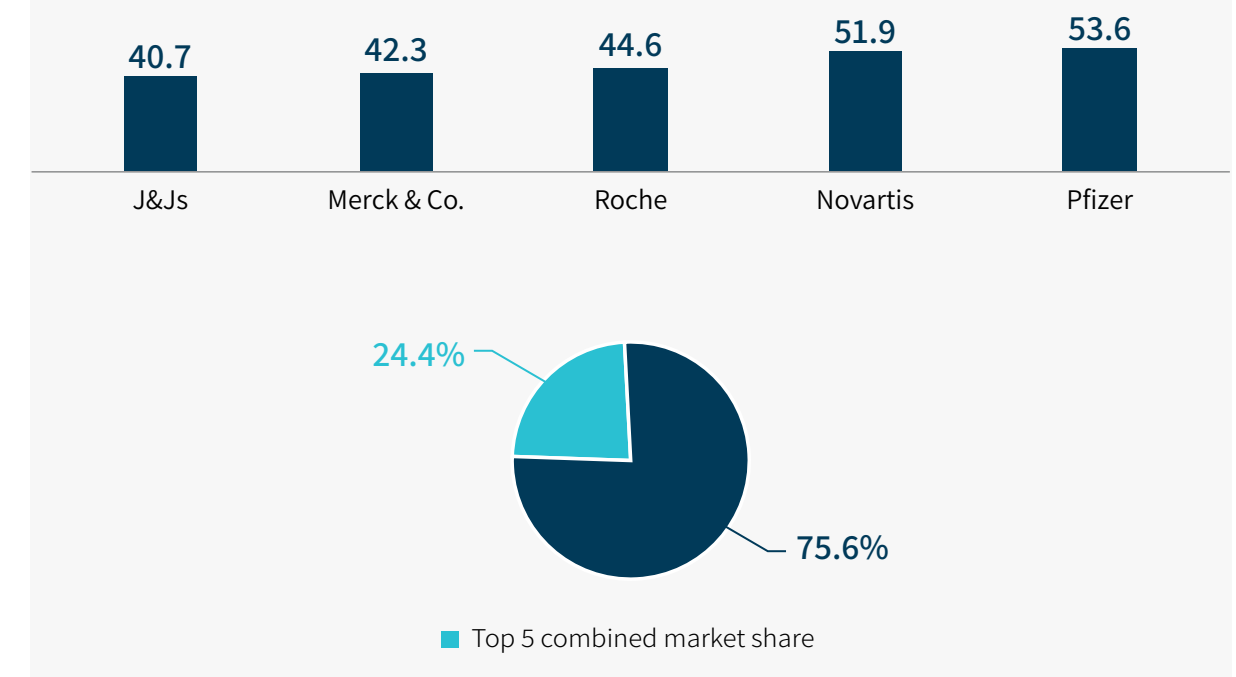
clinical health records based on both community and hospital care, bio-repository with patients' consent/ commission data already embedded, with a relevant sample scale. In addition, we need the proper engineers, statisticians and genomics experts which will work with the data and arrive at new discoveries, along with leading clinicians and skilled professionals from the pharma industry that know our business."

While collaborations between pharma giants and digital therapeutics companies increase, they still hold significant challenges, as mentioned in the last DTx conference in Boston (Sep 2018):

"One of the challenges with digital therapeutics companies is that their mindset is 'How do we sell this as it is?' rather than 'How do we partner with pharma?'"

The statement represents the existing gap between start-ups and healthcare corporates, and their challenge to work together.

FIGURE 5: TOP 5 PHARMA COMPANIES GLOBAL REVENUES (\$USD BILLION) AND SHARE OF GLOBAL MARKET (%), 2018⁹



Pfizer is focusing its digital health efforts in seamlessly integrating clinical trials into the lives of patients through the use of mobile and digital technologies, ranging from electronic consent forms to wearables that enable remote collection of clinical data.

The company is also engaged in several innovative

partnerships that apply digital and artificial intelligence tools to reduce trial time, design more efficient studies, and drive greater access to clinical trials for diverse populations. One particularly interesting partnership is the company's cooperation with Ochsner (a Louisiana based non-profit healthcare system) through formers' innovation lab. The alliance aims to create faster, improved access and connectivity to clinical trials as a result of direct data system integration and using automated study conduct tools.¹⁰

2. GLOBAL PLAYERS' DIGITAL HEALTH PRIORITIES



Novartis is working on proprietary digital health products as well as partnerships and acquisitions. Notable activities during Q3'18 include a partnership with Medidata solutions subsidiary Shift Analytics, to use their data platform. It was involved in joint research with digital health company Healint regarding chronic migraines, and contributed \$30 million to the start-up's funding round.



Roche completed a significant acquisition of approximately \$2 billion for US based Flatiron Health, a market leader oncology-specific EMR in 2018. As previously mentioned, it has a partnership to develop an acute care decision making system with GE.

The acquisition gave Roche more data in the field of oncology, and helped it leverage its research abilities and efficiency.



Merck is focusing its digital health efforts in China, and has allied with Alibaba Health, a subsidiary of the Chinese internet giant Alibaba. As a result, Chinese patients only need to scan the barcodes on their medication with a mobile phone. Users then receive the digital package information leaflet along with instructions on how to take the medication as well

as details on the disease and the drug itself. Other than tracking and tracing drugs, the joint health platform with Alibaba will be used above all for online health services in therapeutic areas such as diabetes, thyroid disorders, colorectal cancer and cardiovascular diseases. China is an especially attractive market for digital healthcare, due to its large population, enormous size and advanced IT infrastructure.



J&J has both medical device and pharmaceutical offerings, and accordingly has similar traits to both sector. Some of its key initiatives include its health partner platform, which will give patients preparing/recovering from surgery access to digital health solutions, in order to improve medical adherence. It recently made a significant acquisition of over \$1 billion to incorporate a digital surgery company Auris Health.¹¹

Janssen pharmaceuticals, its pharma related business, takes part in the 'beyond the pill' trend, and utilizes a build or buy strategy. It has both developed an app as part of its partnership with Memo, as well as a similar app for baby sleep monitoring on its own (J&J Bedtime). It also funds digital health studies, including wearable sensors and artificial intelligence at Haga teaching hospital in the Netherlands, incorporating technology from startups Vital Connect and PhysiIQ.

J&J's Vice President External Innovation summarized its key priority areas in the digital health sector:

"We have a significant effort in digital surgery. We want to provide digital tools to enhance and expand surgical procedures, and assist with decision making"



GSK, as well as other pharma giants is highly interested in digital therapeutics.

For example, in Q3'2018 it invested \$300 million in 23andMe, which also provided GSK access to the startup's database. The company aims to use the data to develop an experimental Alzheimer drug.

GSK also made an agreement with NeuroMetrix, to become the wearable pain relief app's US distributor.

Additional activities include Sanofi Ventures investment of \$17 million in Click therapeutics round; Merck's partnership with Healthy Interactions, a population health company for chronic disease management and Otsuka Pharmaceutical's collaboration with Proteus, a digital health sensor carrying pill.

TECHNOLOGY, TELECOM & RETAIL

The digital health market attracts many non-traditional players, which eye the healthcare sector. Technology players aim to leverage their digital and computational abilities to develop healthcare solutions and improve care, mainly offering AI and analytics tools, cyber security and advanced

IT solutions or developing innovating mHealth platforms. An additional sector that is entering the field, though not in the same scale and growth, is the telecom sector, which may offer connectivity and Health-IoT solutions using connected devices to monitor and treat patients.

Retail giants, such as Amazon, aim to use their expertise to disrupt healthcare and impact pharmaceutical supply chain, care management and other initiatives. Alibaba also presents its ambitions in healthcare. Ali-baba's CEO mentioned: *"Our vision is to use big data to improve medicine and the internet to reshape health"*.

These players, among others, also serve as large-scale employers, and aim to create dedicated healthcare insurance plans for their thousands of employees, as shown by the joint initiative of Amazon, Berkshire Hathaway and JP Morgan's JV to create a comprehensive healthcare system, and similarly by US retail giant Walmart. Healthcare growth potential attracts footwear giants such as Under Armour, which launched wellness apps and recently joined forces with IBM's Watson to analyze fitness data and build personalized health profiles.

However, as non-traditional players increase their healthcare offering, they must develop significant partnerships with traditional healthcare providers and tech giants. To enter the digital health market, they need to develop and enhance both clinical abilities, know-how and vast understanding, as well as new market channels in order to enter the elaborate healthcare system.

2. GLOBAL PLAYERS' DIGITAL HEALTH PRIORITIES



Amazon has been experimenting in the healthcare sector since as far as in 1999-2000, when it invested in drugstore.com. Although the investment had limited success, in 2018 Amazon re-entered the field by several initiatives, including a joint venture with JP Morgan & Berkshire Hathaway, the online pharmacy Pillpack's acquisition of nearly \$0.75 billion, and its acquisition of 'Health navigation' in 2019.



Google continues to both develop AI products for a wide range of healthcare fields, as well as to incorporate mHealth solutions as part of its android platform. Google's parent company, Alphabet, already has a vast healthcare portfolio, including Verily life sciences, Google Genomics, Deepmind and Google Fit.



Apple mainly focuses on solutions based on its iPhone capabilities, and sharing of medical records on the iPhone. In 2019 it announced an additional digital health acquisition of Tueo Health, which provides asthma management solutions. This acquisition follows its prior acquisitions of Glimpse in 2016 and Beddit (a sleep sensor maker) in 2017.

Other than the tech giants, telecoms such as Telefonica, Samsung and Deutsche Telekom have developed digital health offerings, although they seem to be lagging behind the tech's substantial growth.

Nevertheless, Telecoms still have significant operations in digital health, for example AT&T launched a digital health lab in Texas in 2016¹² and partnered with IBM Watson as part of Project DOC to manage chronic diabetes and obesity; Telenor launched Tonic in 2016 to offer healthcare information in developing countries; Deutsche Telekom established a new digital health unit in 2017 which explores new products and invests in healthcare related research, for example in the field of dementia.

An additional growth driver for telecoms in Europe, US and Asia is the surge of 'internet hospitals', which require robust connectivity and usually cloud based infra-structure. For example, Deutsche Telekom has set up a digital information system in a German hospital, that enables care givers to access medical records and facilitates collaboration.

HEALTHCARE SERVICE PROVIDERS AND INSURERS

Medical service providers, such as hospitals and community care service, seek to implement digital solutions to better engage with patients, payers and other providers. For example, providing remote rehabilitation, surgery, treatment and consulting, using tele-medicine platforms. They also develop

managed care solutions, mainly to tackle and assist chronic disease management and prevent patient deterioration. An additional priority is to improve their operational and financial stability, by using digital tools to improve internal administration, operation and revenue management. Lastly, many public health institutions, public community care providers and hospitals aim to promote precision and preventive medicine, mainly using data analytics tools to anticipate risk groups, or develop targeted treatments for specific community traits.

Similarly to traditional service providers, many insurers aim to enhance their offering and become service providers themselves, either by acquiring medical facilities, or offering their own treatment solution, for example by providing remote treatment platforms. Some of the insurers are aiming to reduce their cost of care, while some see digital health as an emerging field and a significant growth engine. AXA Group, a European based private insurance network serves as a good example, and has acquired Maestro Healthcare, a digital health company aiming to provide a one stop shop for health benefits management, for \$155 million.¹³

VC FUNDS, PRIVATE EQUITY AND OTHER FINANCIAL INVESTORS

In addition to medical and pharma companies, insurers, VCs (that may behave as a combination of strategic and financial investors), and 'pure' financial investors are significant players in the field, with a growing number of venture funds specializing in health, in particular, digital health.

Those companies aim for start-ups with solid and sustainable ROI. Today, about 50% of the deals, in terms of deal value, are performed by financial investors rather than strategic investors, meaning they should very well be considered as a significant growth engine to the digital health economy.

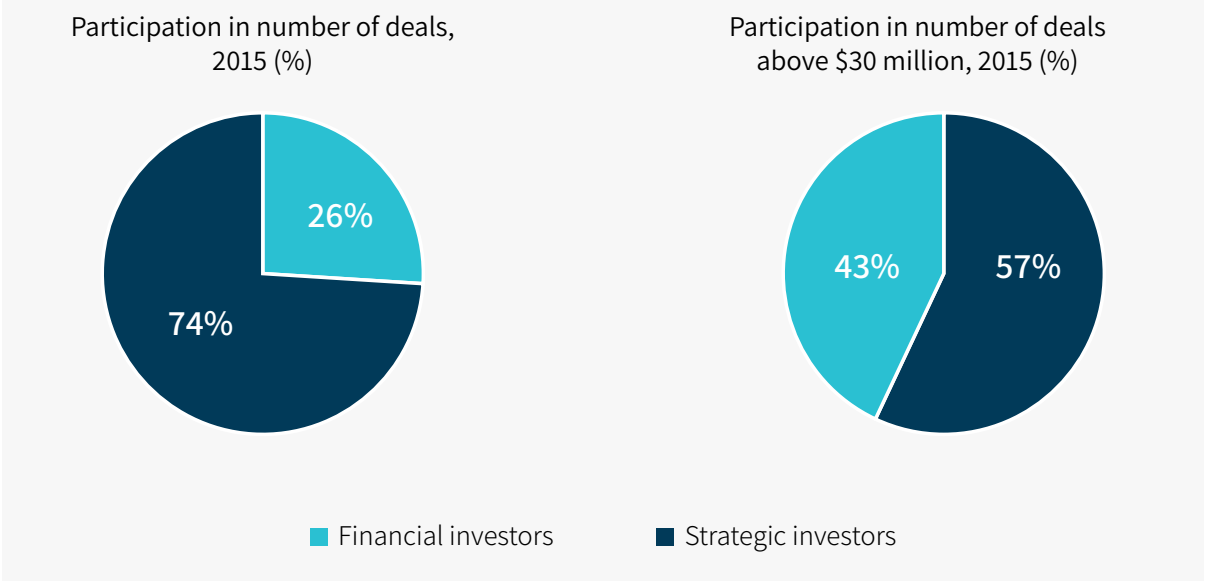
“ The big insurance companies in the US are on a buying spree. They want to engage better with patients and see digital health tools as an opportunity to do so

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2. GLOBAL PLAYERS' DIGITAL HEALTH PRIORITIES

FIGURE 6: ANNUAL INVESTMENTS IN DIGITAL HEALTH ¹⁴



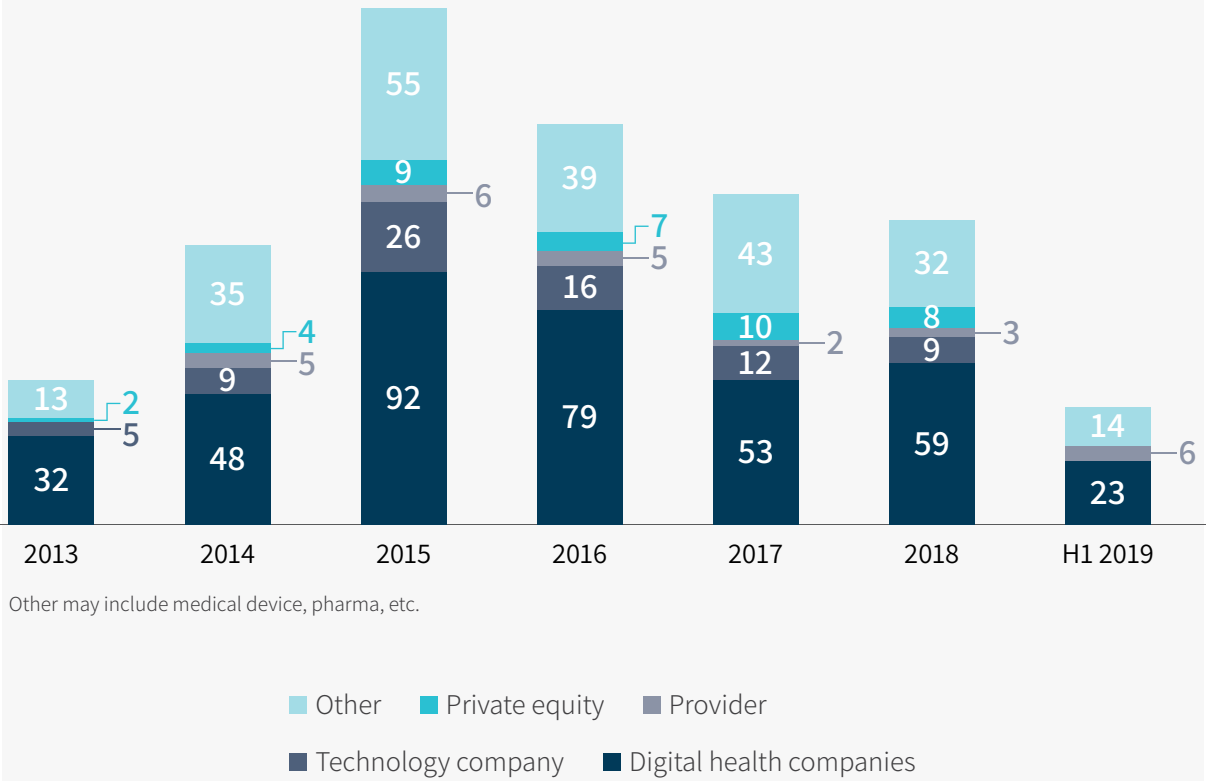
DIGITAL HEALTH / HEALTHCARE IT PLAYERS

The most active consolidators and acquirers in the market are digital health/ healthcare IT companies, which have mature and established products. Although the market is still growing, some market leaders, such as All Scripts & Cerner, Change Healthcare and MDLive already have enough scale to acquire smaller companies and enrich their portfolio. According to Rock Health analysis (see figure 6 below), About 50% of the acquisitions in 2018 (in

terms of acquisition numbers) were performed by digital health players. However, other than several outstanding cases, those acquisitions tend to be smaller than the acquisitions and investments made by pharma, medical device or tech companies.

As the market becomes more mature and more companies will gain scale, this category of players may become highly influential in terms of investments and acquisition of innovation, and should be taken into consideration.

FIGURE 7: NUMBER OF ACQUISITIONS BY ACQUIRER TYPE ¹⁵

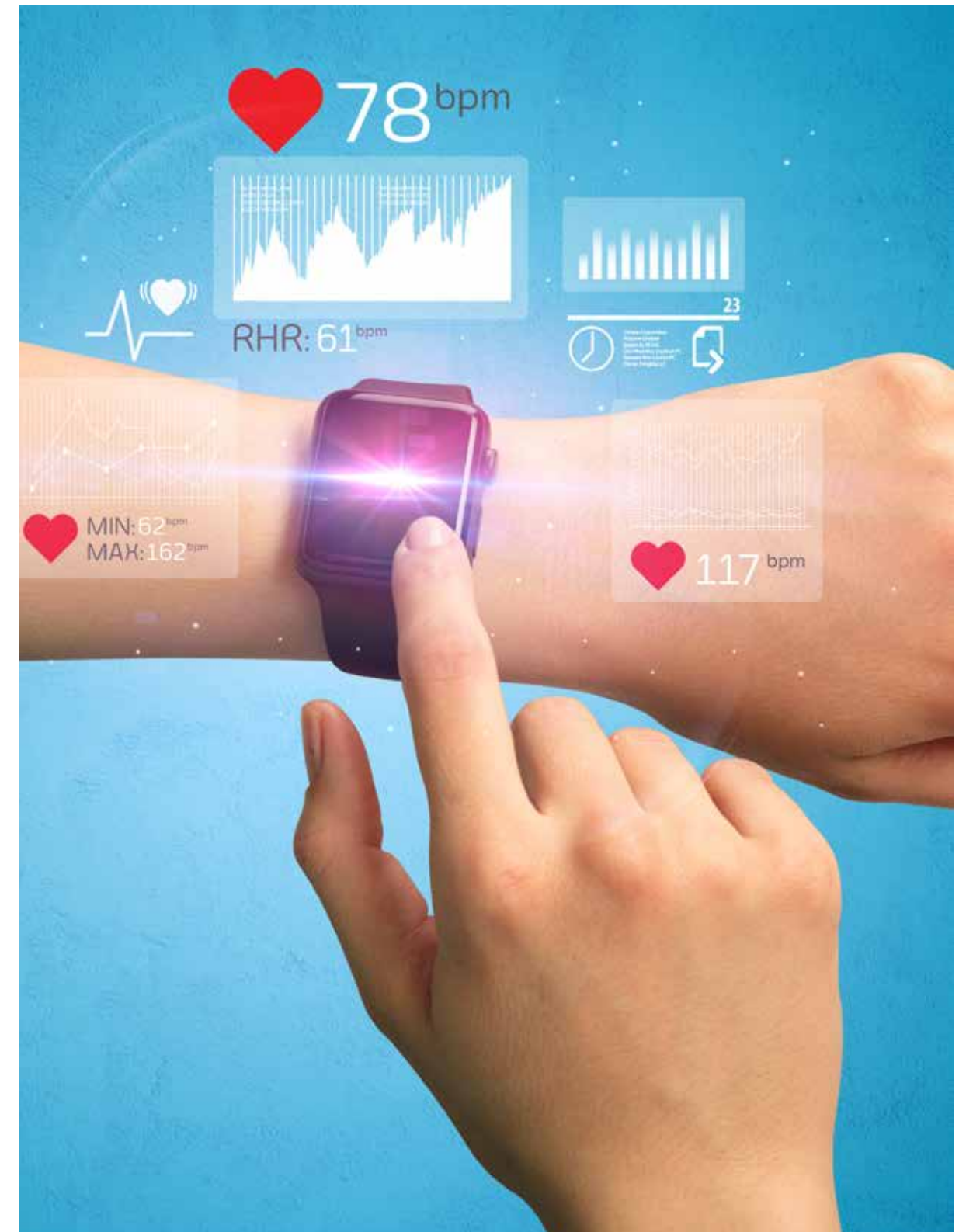


2. GLOBAL PLAYERS' DIGITAL HEALTH PRIORITIES

Notable acquisitions in the last two years by digital health players include:

- Teladoc, a US based telemedicine company, acquired telehealth provider Advance Medical for approximately \$350 million, to increase its penetration to global markets
- EMR giant, Allscripts, acquired patient communication app Health Grid for approximately \$100 million, Practice Fusion for \$100 million, as well as the Israeli company dbMotion which provides interoperability solutions
- Medidata, a US based company which offers cloud and analytics solutions, acquired SHYFT Analytics, which operates in similar fields, for approximately \$200 million

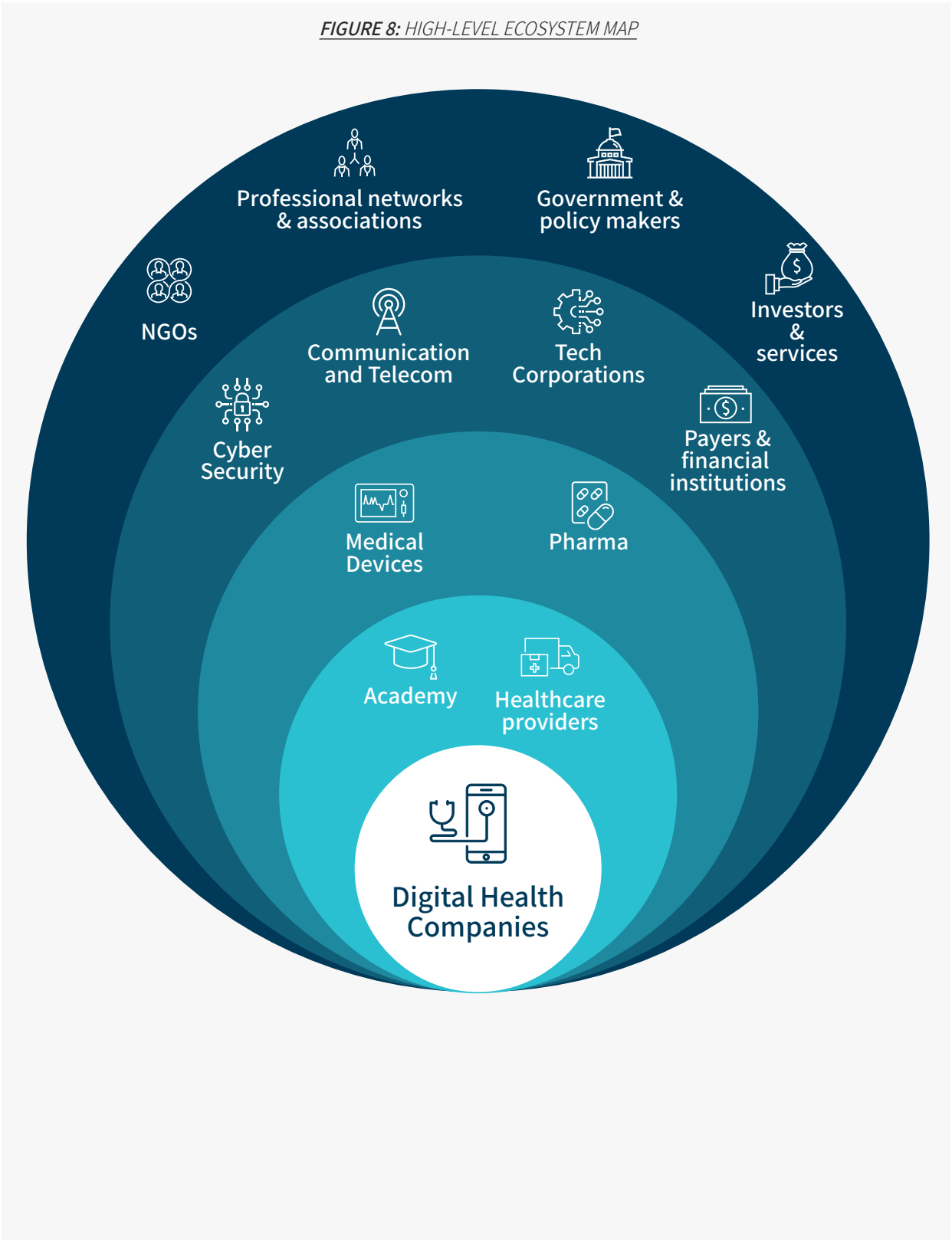
To summarize, the market is characterized by both traditional and new to the healthcare market players. Market leaders from all segments are highly active in terms of investments & acquisitions, although many of the investments, naturally, tend to be domestic based. In the following section, we will review barriers in the digital health field, and evaluate Israel's offering in terms of the digital health priorities mentioned, as well as the barriers to invest and operate for different types of players.



3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

3.1 Ecosystem Overview

Different players within the Israeli ecosystem contribute to the development of digital health solutions, open innovation and fast R&D and deployment. The dynamics and connections between players is a central factor, combining the entrepreneurial culture and the familiarity between people and organizations. The Israeli ecosystem is prone to making the best of what its players have to offer.



3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

3.2 Israeli Digital Health Companies & Core Competencies

The number of digital health start-up companies in Israel has been on the rise since 2011, growing by 15% CAGR. Israeli start-ups are diverse, offering various clinical solutions, including digital therapeutics, remote monitoring, clinical workflow and others. Start-ups develop solutions by leveraging core technologies such as AI, cybersecurity, interoperability & IT integration, VR, IoT and others, as well as serving a variety of digital platforms. Half of these companies already have a developed and clinically proven product at hand, waiting to be deployed on a larger, multi-national scale.

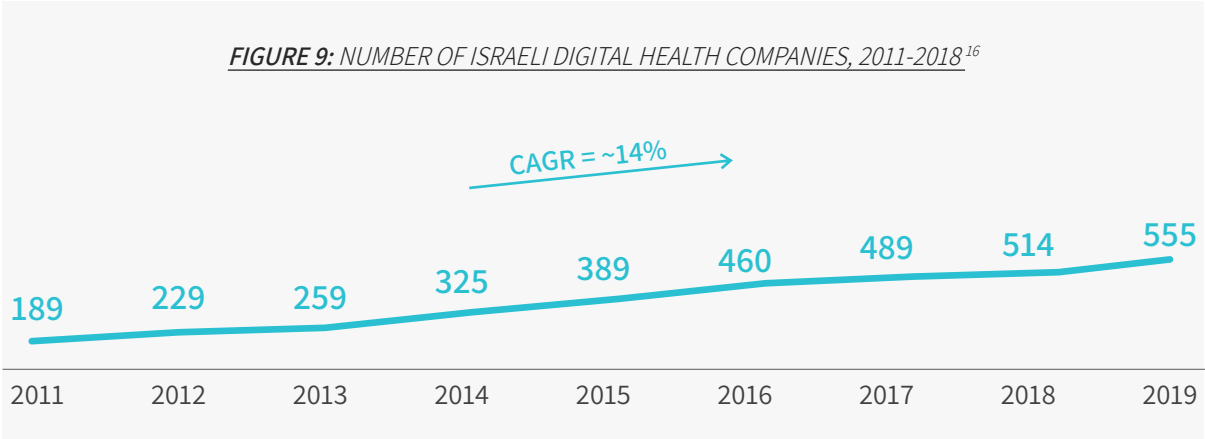
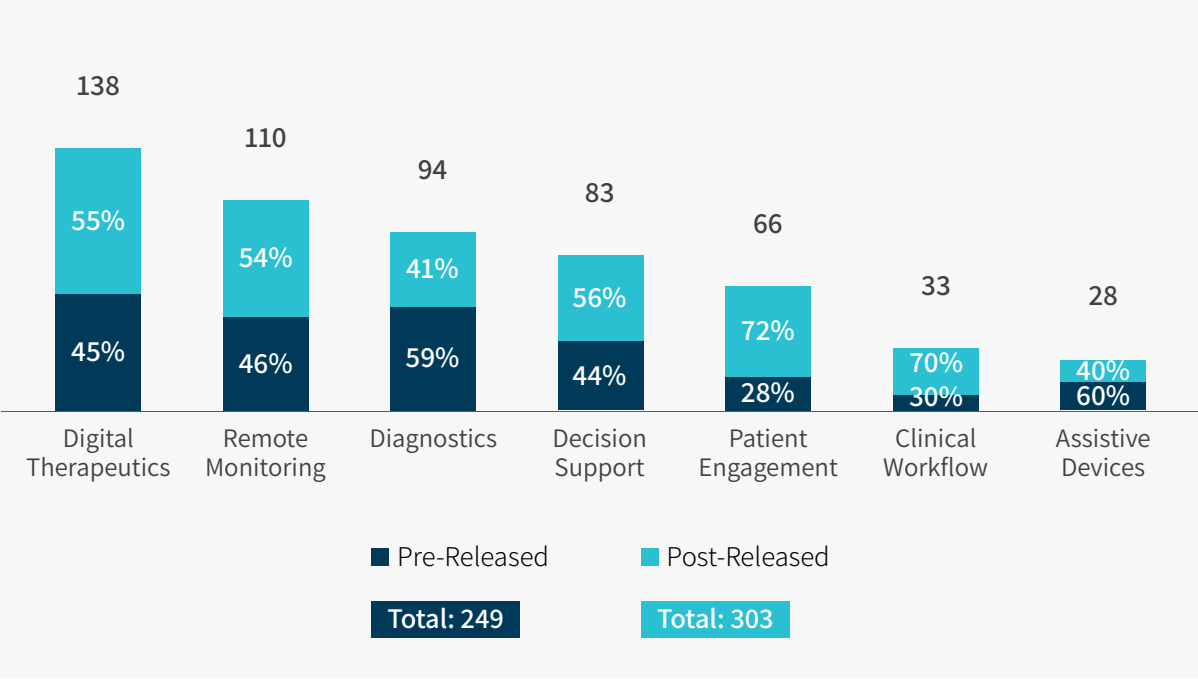


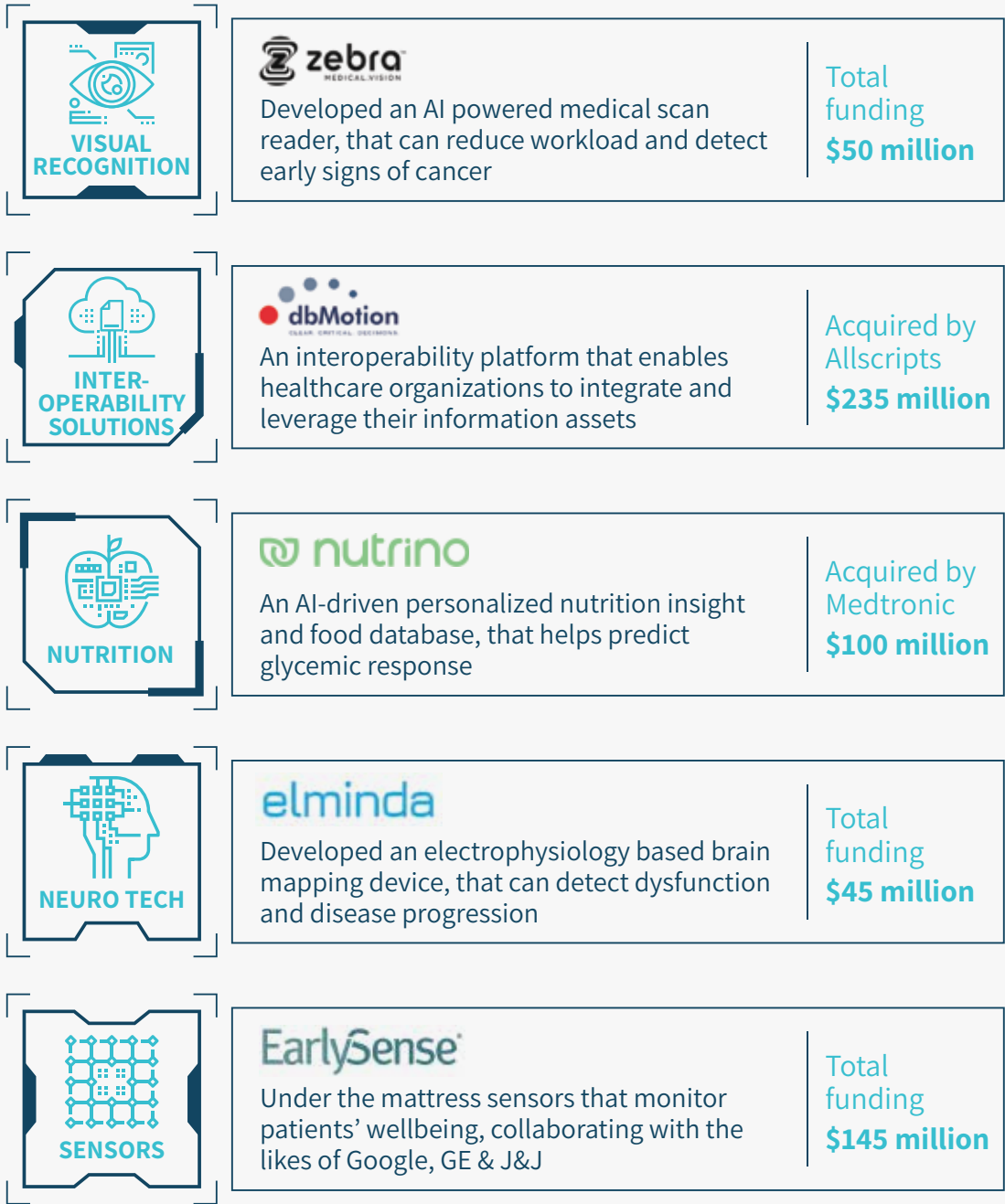
FIGURE 10: NUMBER OF ISRAELI DIGITAL HEALTH COMPANIES, BY RELEASE STAGE AND AREA OF INDUSTRY, 2019 ¹⁷



In addition to the rise in number of start-ups, Israel is home to dominant and innovative players in emerging digital health fields. For example, Israel has several entrepreneurs in visual recognition based analytics, including Zebra Medical Vision, interoperability solutions such as dbMotion; and a core competency in analytics and AI.

3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

FIGURE 11: SELECTED EXAMPLES: DIGITAL HEALTH COMPANIES FUNDING & ACQUISITION AMOUNTS



Israel's thriving start-up ecosystem offers a wide, high-quality deal flow and external innovation opportunities in growing digital health segments.

THE BOOM IN ISRAEL'S DIGITAL HEALTH SECTOR IS POWERED BY ARTIFICIAL INTELLIGENCE

According to the 2019 Global Skills Index Israel is ranked #1 for data science skills, (based on various data science skills). Israel especially excels in machine learning skills (98th percentile), statistics skills (92nd percentile) and statistical programming skills (100th percentile). As a result, over 1,200 artificial intelligence companies have been established in Israel since 2010, and the biggest driver of growth has been data science and analytics. Israel's strong orientation towards AI and Data Science has heavily influenced Israel's digital health sector.¹⁸

Of the \$511 million raised by Israeli digital health companies in 2018, over 50% (\$285 million) was directed to companies in decision support and diagnostics, emphasizing the rise of AI as an industry growth engine. This trend is correlated with global growth trends: machine learning is the fastest growing technology, with 80% YoY global investment growth in 2018.¹⁹

These new technologies have myriad uses, including decision support tools for physicians, medical imaging analysis using computer vision, and big data analytics for population health management. A major factor driving AI innovation in Israel is the accumulation of 25 years worth of EMR's, gradually gathered by Israeli HMOs, allowing start-ups an increased ability to train and test artificial intelligence solutions, and partner with HMOs to validate their technology from early stages of development.²⁰

In the preventative care field, start-ups and homegrown HMO initiatives are building digitalized solutions to intervene and protect people from chronic diseases from as early as birth. Examples are Clalit, who's developing tools to monitor and predict acute myeloid leukemia risk, and Maccabi, that presented an AI system that is able to predict the presence of colon cancer from a simple blood test.²¹

In decision support systems, the wealth of anonymized patient data accumulated in the Israel ecosystem serves as a basis for developing automated diagnosis tools that represent the future of medicine. For example, a DSS was developed by Zebra Medical and Aldoc. The companies, along with other partners, developed an automated radiologist solution to support medical providers through data and diagnostics.²²

In the area of personalized treatment, Israeli data in EMRs is opening new possibilities for truly personalized medicine. Drug discovery makes use of scans of huge genomic and clinical data sets in order to identify new target sites that are specific for certain population groups. In the Israeli industry, there are already several companies using this drug discovery method. Ayala Pharmaceuticals developed a personalized treatment for a specific group of cancer patients carrying a genetic mutation, based on a diagnostic marker that is identified through clinical and genomic data. ImmPACT-Bio, which the Israel Innovation Authority supported through the FutuRx incubator, is developing a CAR-T technology - a treatment in which a patient's T cells are changed so they will attack cancer cells. The treatment will be

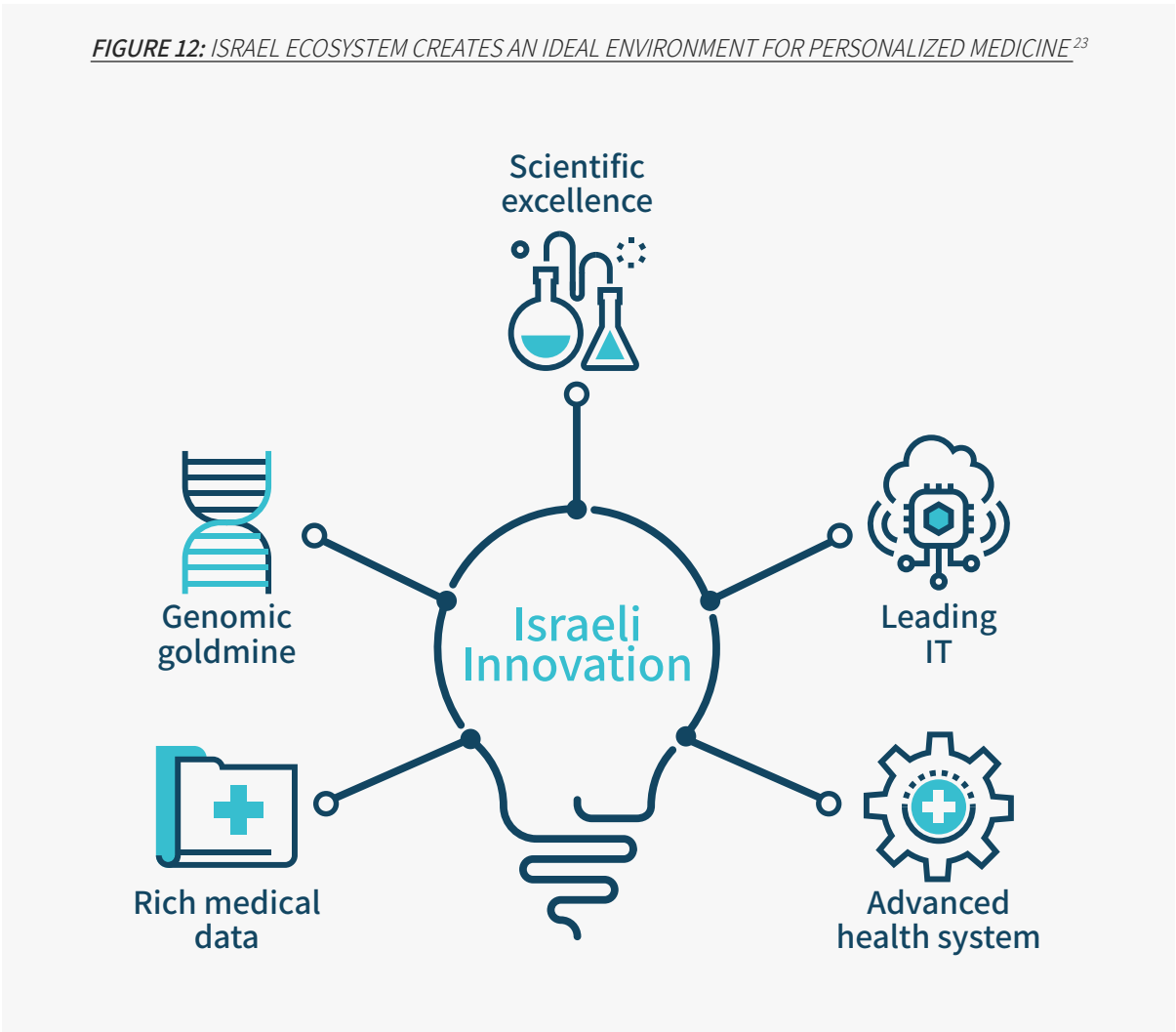
3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

personalized to each patient based on bioinformatics tools and databases of patients' samples.

A third example is CytoReason, which aims to discover drugs using machine learning models applied to biological data of the immune system. Lastly, FDNA, another Israeli company, is leveraging AI to detect physiological patterns that reveal disease-causing genetic variations.



FIGURE 12: ISRAEL ECOSYSTEM CREATES AN IDEAL ENVIRONMENT FOR PERSONALIZED MEDICINE²³



3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

3.3 Healthcare Service Providers, Research and Academic Institutes

Healthcare providers and research and academic institutes play a key role as innovation accelerators and partners for R&D and deployment initiatives. Israel has a high quality national healthcare system, managed and regulated by the Ministry of Health (MOH), which is considered one of the most efficient healthcare systems in the world(Ranked 7th in Bloomberg's 2014 efficiency score).²⁴

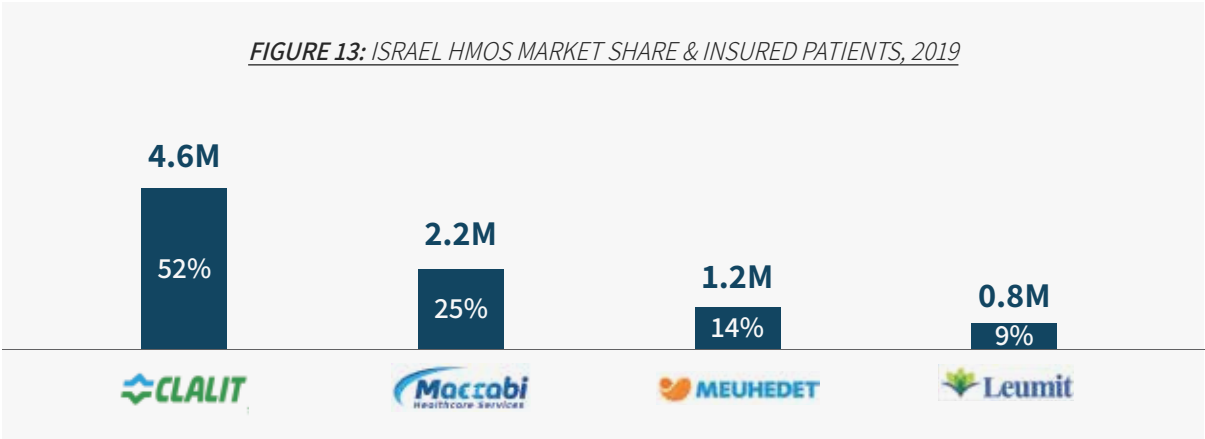
The system is based on a mandatory tax-funded national health insurance (NHI) that covers all Israeli citizens.

The NHI spans over a wide range of medical services – from primary care to complex surgeries provided

by two main caregivers: Israel's Health Maintenance Organizations (HMOs) and hospitals.

ISRAEL'S HMO - COMMUNITY HEALTHCARE SERVICES PROVIDERS

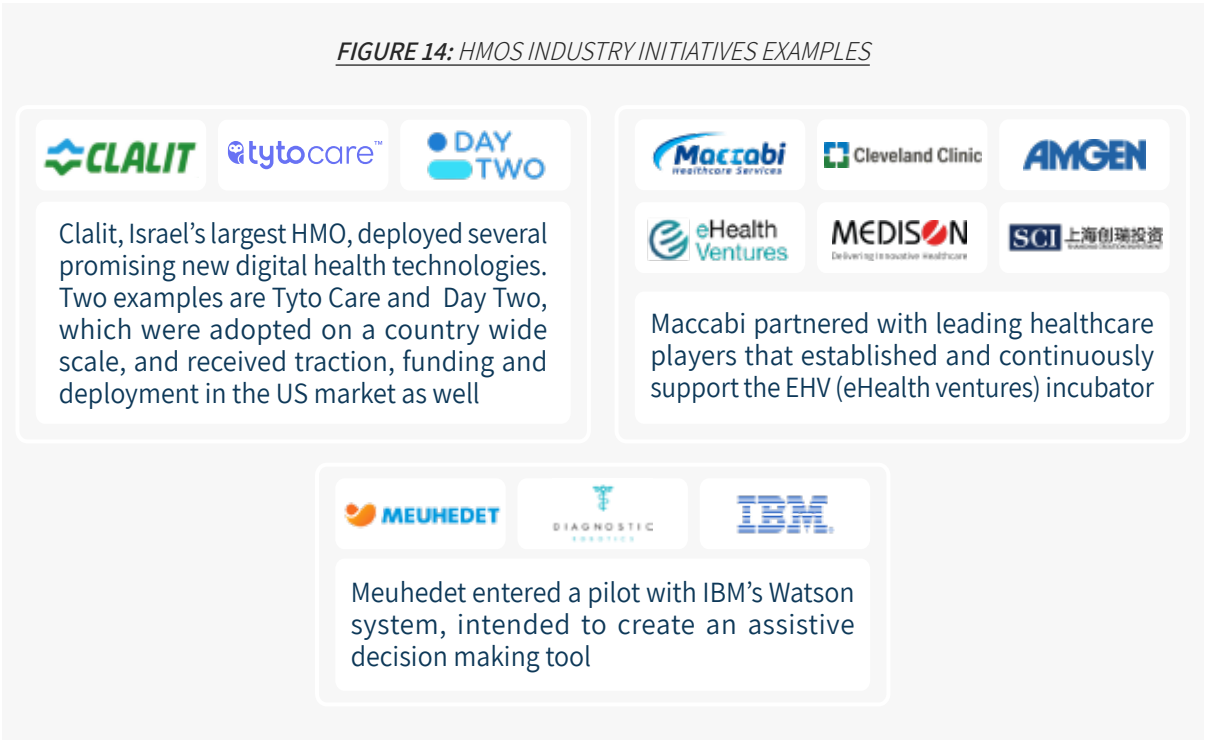
Israeli HMOs are responsible for the provision of community level primary care, and serve as insurers of 98 % of Israel's inhabitants. There are four HMOs in Israel, providing the first line of treatment for non emergency cases through nationwide clinics. They employ expert physicians in various medical fields and own and operate the necessary facilities to provide medical and para medical services to their communities.



HMOs are considered innovative even in international standards, and offer two significant advantages for global collaborators:

1. BETA & DEPLOYMENT SITES

The Israeli HMOs foster innovation by offering various products and digital solutions to manage their patients' health and prevent deterioration. The HMOs operate innovation hubs for early stage start-ups and help them reach first pilots and deploy in nationwide scale within relatively short time cycles.



3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

2. CLINICAL RESEARCH CENTERS

As the HMOs hold large and lifelong databases, they have developed research centers and other research initiatives which aim to develop personalized medicine solutions, as well as decision support systems. The most evident examples are Clalit & Maccabi's research centers. Meuhedet and Leumit, the smaller HMOs, are also the process of improving their research abilities and access to data.

Back in 2010 Clalit established a public health research institute that includes physicians, epidemiologists, statisticians and data scientists, who research and build algorithms based on Clalit's vast databases to improve population health. For example, in 2012 Clalit launched a predictive rehospitalization model that reduced readmission by 12%.

Maccabi's research center also promotes public health research, focused in high priority areas. One of its main accomplishments was a recent development of a technology that predicts colorectal cancer in patients that were not directly examined, based on the information that is collected regularly in the HMOs medical records.

ISRAEL'S PUBLIC HOSPITALS

Israel has three nation-wide hospital chains, as well as several non-profit hospitals. These hospitals are critical for the understanding of needs, the ability to develop ideas and the possibility to test innovative

solutions in partnership with highly engaged and interested potential beneficiaries of the products.

The Israeli government owns 24 medical centers: 11 general hospitals, 8 mental health centers and 5 geriatric centers. Among those are: Sheba in Ramat Gan (~1500 beds) which was recently included in the list of the 10 best hospitals in the world: Tel-Aviv Souraski Medical Center in Tel-Aviv (Ichilov) (~1,200 beds); and Rambam in Haifa (~1,000 beds). In addition to the big urban hospitals, the chain also includes smaller community and rural hospitals, which each have a specific center of excellence and engage in research and innovation.

Recent advances include the establishment of the division for government medical centers, which serves as the chains managing body and provides a single-point of access to the chain's wide resources. In addition, the chain's hospitals are the only ones in Israel which include general health, mental health and rehabilitation services. Today those only exist in Sheba, but are expected to increase with the future merger of Asaf Harofeh general hospital (~900 beds), Be'er Ya'akov mental health center (~450) and Shmuel Harofeh geriatric hospital (~350 beds).

Clalit owns 14 medical centers: 9 hospitals, 2 mental health centers and 3 geriatric centers. Clalit's hospitals include Rabin campus (~800 beds), which is among Israel's leading hospitals; Schneider, a unique model of children's hospital: and Soroka (~1,100 beds), which serves the southern part of

Israel. Clalit's hospital chain's is highly efficient and centralized, and is focused on patient centered care and improving the connection between community and healthcare. It also has a vast and efficient EMR system, which is common to all hospitals, unlike other chains in Israel which are now preparing those platforms. As mentioned, the chain is connected to Clalit's research center, and provides full datasets from both community and hospital care.

Additional chains include Assuta, Maccabi HMO's subsidiary, which owns 7 medical centers: 4 hospitals and 3 community medical centers. Most of Assuta's centers are located in the center of Israel with the far most centers located in Haifa and Ashdod. In addition, most of the hospitals offer private services rather than public, except for Ashdod. Assuta offers a high standard of care and an efficient treatment sequence, based on its integration with Maccabi's community services.

Other than the three main chains, other individual, non-profit hospitals operate in Israel, which serve a wide range of research and innovation opportunities. Among them are Hadassah (~1,000 beds) and Shaare Zedek (~800 beds), both located in Jerusalem.

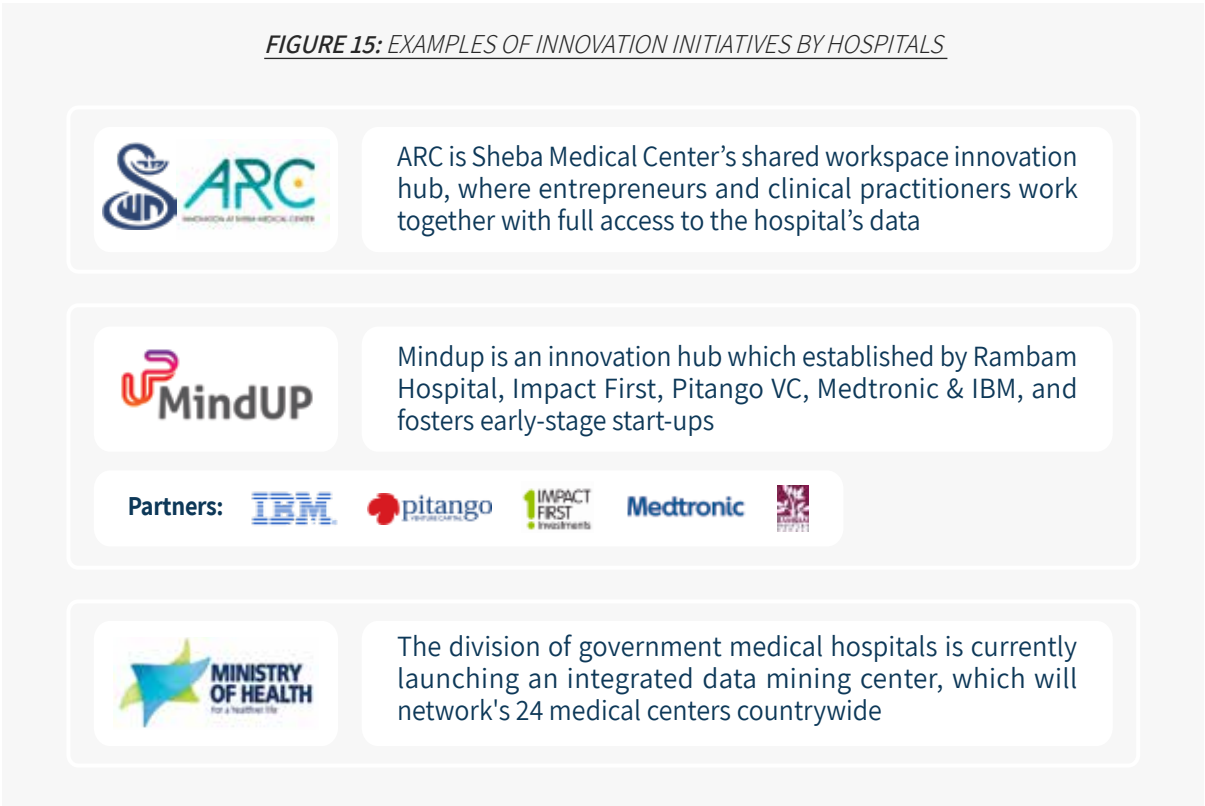
Israel's hospitals are also key participants in the ecosystem, and offer significant advantages to digital health players. Today, most of the hospitals vastly engage in research and have Technology Transfer Offices (TTOs) that assist in commercializing ideas and engaging with industry partners.

Many of the hospitals encourage innovation and industry partnerships. In recent years many of them have developed innovation hubs to promote both small start-ups as well as partnerships in clinical trials and development with established players.

Lastly, similar to the HMOs, Israel's two leading hospital chains – Clalit and the government owned medical centers – are spread throughout Israel and provide care to a variety of populations. As a consequence, this includes remote and rural populations with multiple ethnic and genetic backgrounds. This could serve as an excellent platform to develop digital therapeutics, remote monitoring and diagnosis technologies, as well as using hospital stored data, along with advanced analytics skills, for future developments and clinical trials. It is also relatively easy to engage with both chains through a single POC (either Clalit's management or the division of government medical hospitals) to connect and scale up joint projects.

3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

FIGURE 15: EXAMPLES OF INNOVATION INITIATIVES BY HOSPITALS



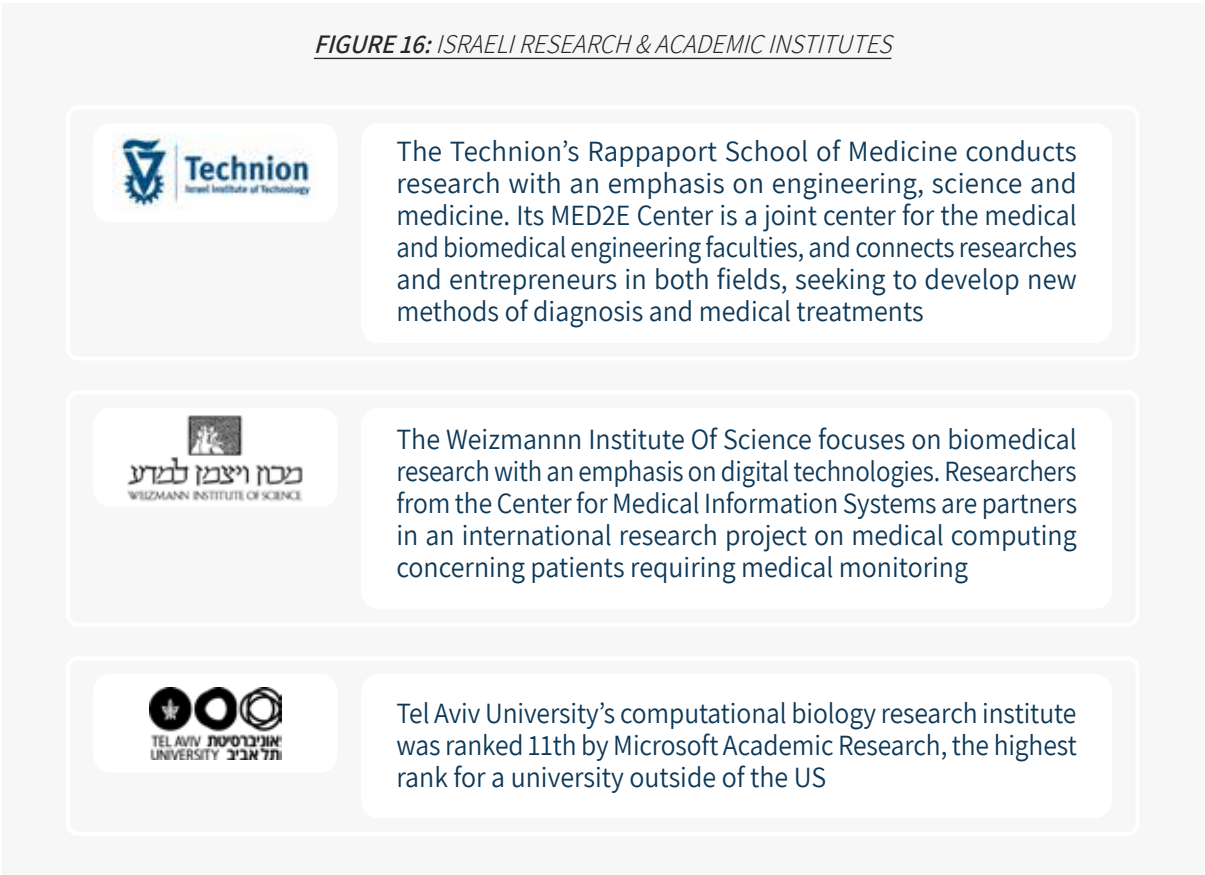
It is important to point out that similarly to Clalit's research center, the government network of medical centers is currently establishing a first of its kind joint Data Mining Center. It will provide service to all hospitals in the network and enable data based research into clinical questions.

ISRAELI RESEARCH & ACADEMIC INSTITUTES

Israel's research and academy have a major impact on the development of the digital health eco-system, as they help develop knowledge platforms and serve as valuable information sources for future industry developments.

For example, the Israeli academy served as incubator for Teva's Copaxone (immunomodulator currently used to treat multiple sclerosis) and Mobileye (vision-based driver-assistance systems). The combination between Israel's strong academic skills in life science, as well as established connections to the industry, positions it as a leading candidate to grow the next breakthroughs in the digital health world. Many of the leading universities are already operating in the fields of health & life-sciences technologies, combined with statistics, mathematics, computer science, etc. In addition, there is a joint national effort to further encourage the Israeli academy's ability to foster digital health innovation and grow more digital health related talents.

FIGURE 16: ISRAELI RESEARCH & ACADEMIC INSTITUTES



3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

3.4 Medical Device & Pharma Companies

Other than the digital health field, Israel has a mature innovation ecosystem, which includes companies and industries that already developed significant global footprints, thus providing valuable advantages, including: top tier management talents, with international industry know-how, substantial presence in newer technology fields such as IoT, autonomous vehicles, and more importantly – life sciences and medical equipment. There are market leaders in additional industries, such as cyber security, software and homeland security. Both private sector companies, as well as the IDF and homeland security companies can add significant value to foster digital health growth.

Israel's medical device and pharma industry includes several domestic players which started as small companies during the 80s or 90s, and have established a significant global presence (examples include Teva, Lumenis, Syneron and Alma lasers).

In addition, many of the major global leaders in medical devices and several pharma leaders in the pharmaceutical industries operate in Israel. Most of them started operating in Israel through an acquisition or partnership with an established Israeli player in the past 20 years. In recent years, the global companies have been expanding their presence through reoccurring acquisitions of established product lines, investments in digital health funds and opening of new innovation centers.

The evolved medical device and pharma industry generates highly skilled talents with a deep understanding of the life science fields, as well as the ability to make acquaintances with global business-makers in the life-science industry. In addition, these companies can quickly adopt innovation and scale it up, and help mentor and foster new start-ups to accelerate their global growth.

FIGURE 17: SOME OF THE INDUSTRY PLAYERS OPERATING IN ISRAEL



3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

3.5 Tech, Telecom, Cyber Security & Homeland Security

TELECOM, TECHNOLOGY & SOFTWARE

These industries are becoming highly relevant to the digital health field, as the need for connectivity, M-IoT (medical internet of things), cloud and advanced analytics solutions among healthcare payers and providers is on the rise. There are several global leaders in Israel in these fields, as well as multi-national players, which are actively engaging in the healthcare sector and developing dedicated digital health activities based in Israel.

CYBER SECURITY & DEFENSE INDUSTRIES

Israel is a global leader in the cyber security sector, as Israeli cyber companies raised 20% of worldwide investments during 2018. A big part of the Israeli dominance is owing to the strong connections between elite IDF intelligence alumni and the tech industry. Furthermore, this industry grew around Israel's advanced defense industries which constitute fertile ground for innovation and relevant developments. As it appears to be, this fertile entrepreneurial environment is in turn enriching the medical tech sector.

FIGURE 18: KEY PLAYERS IN THE ISRAELI ECOSYSTEM



3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

3.6 Government Support & Open Innovation Organizations

The Israeli ecosystem has a wide range of organizations driving digital health forward.

MAJOR GROWTH ENGINE: ISRAEL'S NATIONAL DIGITAL HEALTH ECOSYSTEM

Digital health is regarded as a major growth engine for the Israeli economy. The Israeli government launched in 2018 a national program to accelerate the growth of the digital health industries and capitalize on Israel's assets. The plan's budget for the next 5 years is approximately \$275 million. The plan was built as a cooperation between the relevant government agencies, which have joint targets, collaboration processes and measurements to see the expansion of the program. Key strategic moves, to be promoted by the different agencies include:

- Promoting better access to Israel's unique medical records datasets, stored in HMOs and medical centers
- Creating incentives to improve collaboration between academy, industry and health organizations
- Increasing supply for skilled data-scientists, researchers and other necessary positions
- Assisting Israeli start-ups to grow and achieve

scale, but easing their access to first pilots with Israeli and global healthcare providers

- Promoting foreign investments in Israel's digital health ecosystem

The key participants in the program are the Prime Minister's Office, Digital Israel Initiative, The Ministry Of Health, The Ministry Of Finance, The Ministry Of Economy, The Innovation Authority and The Council For Higher Education.

Although many of the strategic moves were already promoted, the main change achieved by the program was the strong focus and high priority each agency was asked to provide for the digital health sector. It is important to note that the most relevant agency for investors who wish to get to know Israel's ecosystem and better understand the opportunities available, is Invest in Israel, accompanying The Ministry Of Economy, which serves as a first gate to multi-national organizations, accompanying them through the complex Israeli system and bureaucracy.

OPEN INNOVATION DRIVERS: NGOS, NETWORKS & ASSOCIATIONS

NGOs are an additional major factor in driving innovation in the Israeli start-up scene through actively creating partnerships and connecting the ecosystem and those who want to interact

with it. These organizations serve as a gateway for companies looking to engage with the ecosystem. Start-Up Nation Central, for example, offers a wide database which maps digital health companies by sub-sector, and offers information regarding the industry as a whole, helping start-ups to engage with market leaders and promoting Israeli tech worldwide.

In addition, there are organizations that promote and strengthen the connection between organizations, industry participants and market leaders, such as The Israeli Export and International Cooperation Institute, 8400 and HealthIL, Which aim to create effective professional networks in Israel and with global partners.

FIGURE 19: EXAMPLES OF NGOS, NETWORKS & ASSOCIATIONS




3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

ISRAEL'S VENTURE CAPITAL AND INCUBATORS SUPPORT OPEN INNOVATION


The Israeli digital health ecosystem also consists of a wide array of players that support start-ups at the different growth phases, both through funding, aiding to develop the right business models and market access strategies. They also connect to

wider networks of global leaders, which are usually co-investors in these funds. There are many funds that specialize in digital health and have significant expertise in the field. From the multinationals' side, the funds help corporates to engage with small scale innovation, by screening and evaluating high quality technology, and helping start-ups be more aligned with the corporates' needs.


FIGURE 20: EXAMPLES OF FUNDS AND FINANCIAL INVESTORS




aMoon is a leading HealthTech & life sciences venture fund, which operates three specialized funds: a mid-to-late stage life-sciences fund, an early-stage and late-stage fund and an early-stage fund focused on highly disruptive healthcare technologies



OrbiMed invests across the global healthcare industry, from seed-stage venture capital to large publicly-traded companies. Investments are made in one of three strategies: public equity, private equity, and royalty opportunities



Triventures is a venture capital fund focused on MedTech and digital health, which invests in early to late stage opportunities in Israel, US and Europe



Pitango has a wide global presence and invests in various industry segments, including healthcare

FIGURE 21: ADDITIONAL EXAMPLES OF FUNDS AND FINANCIAL INVESTORS



In addition, innovative investment models, which foster open innovation and connect VCs and healthcare providers are on the rise. Key examples include Triventures ARC – a JV by Triventures, one of Israel's largest VCs, and ARC, Sheba Medical Center's innovation hub, and ALIVE HealthTech Fund by Therapix Biosciences, CBG AM, Maccabi and Assuta (Israel's 2nd largest HMO and its hospital network branch).

Other than VCs and service providers partnerships, Israel is also rich with incubators, which are based on Israeli service providers and industry players, or several industry players together. Key examples include Sanara, a joint venture between Philips and Teva; EHV- Maccabi's incubator, partnered with Amgen, Medison Pharma, etc. and Mindup, Rambam Hospital's partnership with IBM, Medtronic and Pitango VC.

FIGURE 22: A SAMPLE OF INCUBATORS THAT HELP DEVELOP HEALTHCARE START-UPS, SOME SPECIALIZE SPECIFICALLY IN DIGITAL HEALTHCARE.



3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

3.7 How can Israel's offering meet the needs of global players?

SUMMARY: THE ECOSYSTEM'S KEY ASSETS



VIBRANT START-UP COMMUNITY

Over 500 active digital health companies, operating in a variety of digital health fields, half of which are in post-release stage and have a clinically validated and tested product



OPEN INNOVATION OPPORTUNITIES

Multiple organizations that help companies understand Israel's potential assets, offering a knowledge base and networking opportunities; local VCs, innovation hubs and accelerators assist with access to high quality deal flow and identification of investment opportunities



PARTNERSHIP AND CHANNEL OPPORTUNITIES

Increasing number of domestic & global healthcare industry players, as well as a mature tech environment, which encompasses strong AI & analytics players, as well as cyber security global leaders, well connected and located within short driving distance, as well as municipal innovation hubs



ACCESS TO PAYERS & PROVIDERS

High quality and life-long community & hospital care; access to 25 years of accumulated, identified and digitized data across providers; leading research institutes and established academy connections; vast pilot & deployment opportunities, all centered within 3-4 hospital chains and 4 HMOs



HIGHLY ENGAGED GOVERNMENT

Digital Health as a Growth Engine government initiative which encourages policy makers to promote digital health. Many agencies offer risk-sharing plans to international corporates that wish to grow their presence, as well as end-to-end personal account management to mitigate regulatory barriers

WHY IS ISRAEL AN ATTRACTIVE LOCATION FOR GLOBAL PLAYERS SEEKING TO INCORPORATE INTERNAL & EXTERNAL INNOVATION IN DIGITAL HEALTH?

Israel's offering is highly attractive for most players' needs and motivations, and provides a relatively low risk and high quality digital health development platform.

First, the cost of end-to-end innovation is relatively low in Israel, comparing to similar costs in the US. The cost of clinical trials and market testing is relatively low, and development cycles are relatively fast. Within 3-4 years, an early-stage company can evolve from initial idea stage to product and with first deployment within a healthcare system that serves over a million patients, as evident in Israel's HMOs and hospital networks.

Second, the new Digital Health as a Growth Engine governmental plan has made inroads in focusing regulatory and policy makers' agendas to promote digital health, and many agencies offer dedicated risk-sharing plans to international corporates that wish to grow their presence, in terms of incentives to open R&D centers, access to data and pilot opportunities (vis-à-vis the Innovation Authority, Digital Israel initiative and the Israeli Ministry of Health) and end-to-end client management as offered by Invest in Israel, to help companies navigate and locate the right incentive plan to meet their needs.

Third, there are many organizations that help companies understand Israel's potential assets, for

example Start-Up Nation Central, IATI, the Innovation Institutes' HealthIL initiative, 8400 network and mHealth Israel, which offer knowledge bases and networking opportunities. In addition, local VCs such as aMoon fund, Orbimed, Triventures & Sanara ventures, along with accelerators, incubators and innovation labs such as MindUp, EHV & ARC, assist with access to high quality deal flow and mitigation of investment opportunities which meet the relevant needs, clinical priorities and business models for various players.

WHICH INNOVATION OPPORTUNITIES EXIST IN ISRAEL'S ECO-SYSTEM AND HOW DO THEY MEET CORPORATES' NEEDS?

1. INNOVATION HUBS & R&D CENTERS

Israel offers several opportunities: for example, Haifa has been nominated the capital of digital health in Israel, and offers a life science ecosystem which includes leading hospitals, HMOs, the Technion – Israel's leading engineering institute – and dominant tech, medical device and pharma players. Those also include vast municipal and NGOs support to bolster opportunities and increase open innovation abilities between players. Various players have established innovation hubs and development centers in Israel, and keep expanding their presence, while leveraging government tenders and opportunities, such as the latest multinational R&D centers tender launched in 2018 by the Israeli Innovation Authority. For details regarding companies' innovation & R&D centers see Chapter 4: Selected Case Studies.

3. ISRAEL'S DIGITAL HEALTH ECOSYSTEM

2. CROSS INDUSTRY PARTNERSHIPS

Israel offers endless partnerships and networking opportunities within a small territory, as it is possible to cross the country end to end within a five-hour drive, and reach leaders and experts within a few calls. High connectivity and accessibility are key success factors to open innovation.

As previously mentioned, digital health brings traditional and non-traditional players together, and requires the formation of JVs and partnerships between corporates that bring together a complementary set of skills to create new products and services.

For example, GE Healthcare and Roche have formulated a new partnership of decision support systems for acute care and oncology, using data analytics and deep learning abilities (more details in Chapter 4: Selected Case Studies). Partnerships between dominant tech players and health service providers are also on the rise, as tech players which bring their digital and computational capabilities seek to develop their products using clinical facilities and knowledge from service providers, and combining this with existing portfolios of industry players along with market access and channels.

Israel has both an increasing number of healthcare industry players, as well as a mature tech environment, which encompasses strong AI & analytics players, as well as cyber security global leaders, two of the most growing segments in digital health. The ability to engage with local and global tech leaders, as well as work closely with other multi-national representatives, creates a significant opportunity which meets many players' needs.

3. M&A OPPORTUNITIES & ACCESS TO DEAL FLOW

The ecosystem includes multiple local partners that help global companies identify and access innovation, as well as helping start-ups refine their business and increase their growth, including local and global Venture Capital players as well as accelerators run by healthcare service providers and leading global players.

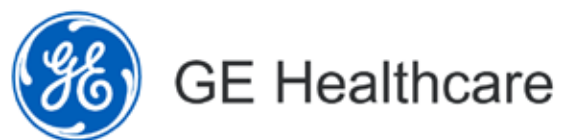
Evidently, a wide range of market leaders, including Amgen, J&J, Medtronic, Philips, GE Healthcare, IBM and others have established a branch of a venture arm, accelerator or a local scouting team, usually as part of a board of directors or partners with Israeli accelerators or VCs. Further elaboration of companies' operating models can be found in Chapter 4: Selected Case Studies.

Israel offers unique assets that encourage the growth of digital health solutions, and a vast range of investment opportunities for foreign corporates. The ecosystem is highly engaged and committed to fostering innovation and economic growth for the sector, supporting both foreign investments as well as local companies in their efforts to scale their solution and bring value to global markets



4. SELECTED CASE STUDIES

GLOBAL LEADERS IN DIGITAL HEALTH ACTIVITY IN ISRAEL



GE Healthcare has a long established presence in Israel, and it keeps expanding it to capitalize on Israel's innovative ecosystem

GE Healthcare started operating in Israel in 1950, and has been growing its presence through acquisitions such as imaging company Elscint in 1996 and Orbotech's nuclear division in 2011. Over the years, GE increased its activity through bolstering its R&D centers and creating end-to-end solutions for the

global healthcare suppliers. Nowadays, the company operates several R&D centers in Israel, with around 700 employees, generating almost \$1 billion in revenue.

With the assistance of the Innovation Authority and other government representatives, GE is building additional development centers in Israel. One of those is intended to be in the field of digital detectors for PET CT activity.

OPENING A JOINT INNOVATION CENTER WITH ROCHE

- GE & Roche recently announced a unique collaboration to develop a decision support system using both in-vivo and in-vitro data to develop AI based decisions for point of care and acute care
- The collaboration is part of their effort to integrate their strong diagnostics solutions into one product
- The collaboration's headquarters is based in the US, and Israel is one of the chosen sites for this unique R&D activity
- The new activity has over 40 employees, mainly developers, specializing in mobile and cloud applications aimed to create precision digital health tools for medical staff

"I made the decision to develop this new activity in Israel the moment I was offered the role. I've previously worked with Israeli personnel; they are known for their quality R&D work but they are great at product as well. Right from the start I had in my mind at least six Israeli specialists I knew who would be great assets for Acute Care" - Paul Mullen | General Manager Acute Care (GE Healthcare in Collaboration with Roche Diagnostics)

SPOTLIGHT

Medtronic

Medtronic increased its presence in the Israeli healthcare innovation market through opening new R&D centers and M&A activity

Medtronic began operating in Israel in 1974, and currently operates R&D, marketing, manufacturing and sales divisions. The company acquired six Israeli companies and startups, in part through the acquisition of Covidien, an Irish global medical

device manufacturer that was highly active in the Israeli healthcare innovation market and helped Medtronic access the market as well.

Notable independent acquisitions Medtronic has made include Mazor Robotics for \$1.6 billion in 2018, and even more recently Nutrino, a nutrition data analytics company, for \$100 million. Today, Medtronic has over 1,000 employees in three different locations in Israel.

CONNECTING WITH THE ECOSYSTEM AND INVESTING IN EARLY STAGE START-UPS

- The acquisition of Nutrino is of a fairly small scale for a giant such as Medtronic, but serves as a significant vote of confidence in the Israeli digital health ecosystem
- Another sign of Medtronic's willingness to engage with Israeli companies early on is its investment in the MindUp Incubator
- MindUp is a digital health incubator, a joint venture of Medtronic with Rambam Hospital, IBM, Pitango and Impact First
- The companies in the incubator get direct exposure to entrepreneurial activity and deal flow, without the hassle and the liability of actually doing that work themselves
- Medtronic CEO - Omar Ishrak, has frequently expressed appreciation for Israeli innovation and activities in Israel, and during his term as CEO, Medtronic acquired Covidien, Oridion Medical, Given Imaging, and superDimension, which it continued developing in Israel

"The history of acquisitions by Medtronic makes their belief in the Israeli ecosystem clear. Medtronic has leveraged Israeli technology to drive positive results for patients and physicians in multiple therapeutic areas" - Yael Glassman | CEO of Nutrino Health

SPOTLIGHT

4. SELECTED CASE STUDIES

GLOBAL LEADERS IN DIGITAL HEALTH ACTIVITY IN ISRAEL

PHILIPS Healthcare

Philips Healthcare operates extensive R&D & product lines in Israel, while becoming a dominant player in the Israeli innovation eco-system

Philips began operating in Israel in 1948, and today holds extensive R&D and manufacturing capabilities. The company's first digital PET CT was developed in Israel, and is currently one of the main production lines.

Today, both R&D centers in Haifa and Petah Tikvah, employ around 1,200 workers, generating almost \$1 billion in revenue. In 2018, the company expanded its activity with the acquisition of EPD Medical that develops inner body navigation for arrhythmia treatment.

Israel is one of the company's five main innovation hubs along with Amsterdam, Shanghai, Bangalore, and Cambridge, Mass.

APPLYING ISRAELI R&D ACTIVITY ACROSS THE VALUE CHAIN AND BUILDING END-TO-END PRODUCT LINES

- Digital health is central to Philips's growth strategy in Israel, focusing on development of interoperability capabilities and medical data management
- Philips has recently announced that it is looking to acquire companies in Israel, specializing in cycle of care, healthcare informatics and diagnostic imaging
- Philips is investing in the local start-up scene through Sanara, an investment platform set up as a joint venture with Israeli pharma giant Teva, focused on various healthcare innovation fields, digital health and healthcare IT amongst its expertise areas

"It helps that Israeli entrepreneurs in the medical technology space also all speak English and have a highly global outlook on business. They know that you don't develop innovation just for Israel but for the world"

"Everyone I met in Israel understand how the healthcare system in the US works and have connections there. That's particularly important for Philips, since the US is our largest market"

- Ryan Bloom | Chief Innovation and Strategy Officer at Royal Philips. Based on an Interview 'Israel 21C', May 6th 2019

SPOTLIGHT

CHANGE HEALTHCARE

Change Healthcare is active in the Israeli digital health market through its growing R&D center and M&A activity

Change Healthcare built its presence in the Israeli market on the basis of Medcon, an imaging company

founded in 1993 and acquired by McKesson (now part of Change Healthcare) in 2005. Today, Change Healthcare operates a R&D center with over one hundred employees in Holon, near Tel Aviv. The Israeli branch focuses on development of data and monitoring for cardiology units.

EXPANDING INNOVATION ACTIVITY WITH GOVERNMENT SUPPORT

- During 2018, Change Healthcare participated in and won a tender by the Israeli Innovation Authority (alongside Medtronic and GE) for the establishment of new R&D centers, dedicated toward the development of the digital health ecosystem
- The decision to apply for the tender was backed up by the familiarity and positive experience of already working within the local ecosystem
- Important aspect of the decision was the confidence Change Healthcare management has and continues to have in the abilities of the Israeli branch management
- The tender framework provided a significant incentive for Change Healthcare's management to take the risk and establish a new R&D center

"The Israeli ecosystem has several great advantages. First, the government is relatively pro industry; they continuously look for new ways to work with multi-nationals and to incentivize them to take a bigger stake in Israel. Second, the available talent is really good; you have teams with expertise throughout the healthcare value chain, and they can deliver end to end products in various fields of activities. Finally, the ecosystem is very intimate, both geographically and personally. This is critical for our style of open innovation" - Omer Schalit Cohen | Head of Change Healthcare's center in Israel

SPOTLIGHT

4. SELECTED CASE STUDIES

GLOBAL LEADERS IN DIGITAL HEALTH ACTIVITY IN ISRAEL



Amgen, a global biotechnology leader, invests in eHealth ventures, an Israeli digital health incubator

Amgen is a US-based company with many affiliates and subsidiaries worldwide. Most of Amgen's core R&D centers are located in the US. Accordingly, up until the 2016 investment in eHealth Ventures, Amgen was not directly active in Israel.

After several scouting tries, during 2018, Amgen increased its Israeli presence through partnering with Entera bio Ltd., an Israeli company, specializing in the oral delivery of large molecules.

INVESTING IN A DIGITAL HEALTH INCUBATOR

- In 2016, Amgen joined major healthcare players such as Cleveland Clinic, SCI (Chinese Venture Capital Fund) and Medison Pharma as a key investor and partner in eHealth ventures (EHV) - a digital health incubator, which serves as Israel's second largest HMO's (Maccabi) innovation and venture arm
- The incubator represents a unique partnership structure with the added value of each member of the consortium being a significant asset, used for the growth of the portfolio companies and the commercialization of their products
- The unique structure of the venture allows deep understanding of market needs, while having a direct connection to Maccabi's unique dataset. In addition, the companies can use Maccabi's network as a beta site to test their products in a real-world, community healthcare environment
- By partnering with EHV, Amgen is able to access Israel's most innovative start-ups' deal flow, assist and shape their commercialization process and speed-up their deployment process - from an innovative idea to a clinically proven, efficient and market oriented product

"This investment reflects the company's deep commitment to innovation which advances modern medicine and the recognition of Israel as a global center for such innovation"

- Corinne Le Goff | SVP Amgen Europe



IBM operates in Israel its biggest digital health research lab outside of the US, while enhancing its ecosystem engagement with incubator and accelerator programs they invest in

The main activity of IBM healthcare in Israel surrounds the Watson healthcare research lab located in Haifa. The lab encompasses IBM's effort to harness a combination of attributes of the Israeli ecosystem: Strong AI knowledge, availability of medical data and entrepreneurial character.

HIGH INTEGRATION INTO EVERY ASPECT OF THE ISRAELI ECOSYSTEM AND ESTABLISHED CONNECTIONS WITH LOCAL HEALTHCARE PROVIDERS

- IBM's research lab is highly integrated into the digital health ecosystem and has multiple partnerships with both Israeli academy and local healthcare providers
- For example, Meuhedet, an Israeli HMO with over 1 million Israeli insurees, implemented IBM Watson solutions to improve its clinical decision making among OB/GYNs, using NLP (Natural Language Processing) applications to analyze and provide recommendations based on patients' electronic health records
- IBM's involvement in building up the ecosystem starts at an early stage, providing scholarships for students exceling in relevant research
- IBM is also a founding partner of the MindUp incubator dedicated to advancing digital health solutions (with Medtronic, Rambam Hospital, Pitango and Impact First)
- IBM is always on the lookout for possible partnerships with other major healthcare industry players and service providers, looking for joint ventures in the field of digital health

"The fact that Israel is a tech powerhouse, helped IBM's corporate management decision to approve incubator and accelerator programs. The well known entrepreneurial spirit of the ecosystem is a major asset" - Michal Rosen-Zvi (PhD) | Director of Health Informatics at IBM Research

4. SELECTED CASE STUDIES

GLOBAL LEADERS IN DIGITAL HEALTH ACTIVITY IN ISRAEL



Microsoft's digital health division operates in Israel based on the vast general R&D centers Microsoft has in Israel

The healthcare oriented R&D activity in Israel grew from the extensive cyber and AI R&D center Microsoft operates in Israel. Microsoft has also been active in Israel through acquisitions, notably that of Adallom,

a cyber defense company purchased for about \$320 million in 2015.

The healthcare dedicated division has operated in Israel for about 4 years and is focused on developing NLP (Natural Language Processing), genomic sequencing and medical imaging solutions for healthcare providers.

MICROSOFT'S HEALTHCARE DIVISION IN ISRAEL KEEPS EXPANDING, PROVIDING SOLUTIONS TO THE GLOBAL CORPORATE

SPOTLIGHT

- Microsoft's R&D center in Israel is focused on using its expertise in AI applications for creating digital healthcare services, both for caregivers and healthcare providers that in turn offer the services to their customers
- The recently launched Microsoft Healthcare Bot, developed in Israel, is a platform for diagnostics based on customer reporting of symptoms
- The development was done in close partnership with major healthcare providers both in the US (Aurora Advocate Healthcare) and in Israel (HMO Clalit)
- Other digital health applications are being developed all the time, and the healthcare division is growing rapidly

"The Israeli team has both the knowledge and the innovative attitude, as well as the execution skills needed to create products. That is what made it possible for us to grow our team and deliver on our mission. Good ideas alone would not have been enough"

- Hadas Bitran | Head of Microsoft Healthcare Israel



AstraZeneca recently launched a Digital Health Innovation hub in Israel, as part of its global network of Health Innovation Hubs

AstraZeneca is a leading global, science-led biopharmaceutical business developing innovative medicines, used by millions worldwide. It opened its local office in Israel in 2008 and has been growing since. AstraZeneca Israel works closely with the

medical community in Israel to promote research and development of medical treatments, and run clinical trials to strengthen the healthcare services provided.

In October 2019, AstraZeneca launched "BeyondBio", a Digital Health Innovation Hub which joins AstraZeneca's Innovation hubs network in locations such as Sweden, China, UK, USA and France.

LAUNCHING "BEYONDBIO" ASTRAZENECA'S INVESTMENT IN THE ISRAELI ECO-SYSTEM

SPOTLIGHT

- BeyondBio is built through strong local partnerships and currently includes two innovative programs:
 1. A partnership with ARC, the innovation campus of Sheba Medical Center to support the creation of innovative digital health solutions.
 2. A digital health accelerator in partnership with Israel-based venture capital firm Jerusalem Venture Partners (JVP); Israel Initiative 2020 (ii2020); The Kahn-Sagol-Maccabi Research and Innovation Institute ; Shaare Zedek medical center and Microsoft. The accelerator will work with local startups to try and solve key challenges of the healthcare sector through digital innovation.
- AstraZeneca connects between Israeli research institutes, health providers, innovators and our network of global innovation hubs. Specifically, with the iCampus innovation campus in Wuxi, China.
- AstraZeneca is exploring the Israeli ecosystem and seeking further opportunities for collaborations.

"BeyondBio is an important addition to the global effort towards innovation by AstraZeneca, This is a combined effort of research and development, digital and marketing that come together to support our strategy of improving patient health and wellbeing around the world"

- Iskra Reic, AstraZeneca executive VP for Europe and Canada

5. ACKNOWLEDGMENTS

- **AIMEE FISHER** - VP strategy & Business Intelligence | aMoon fund
- **ALAN KHOLOS** - Director of Corporate Development, Infusion Solutions | BD
- **ALISA MESH ILIESCU** - Managing Director | MedTech Raanana Innovation Center
- **ANDERS DYHR TOFT** - Innovation executive | Novo Nordisk
- **ANGELA RABINOVICH** - Director, Life Science Department | Israel Export Institute
- **ANISHA SOOD** - Partner | Echo Health Ventures
- **ANYA ELDAN** - VP Startups Division | Israel Innovation Authority
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- **BRUCE R. ROSENGARD, MD** - Vice President, External Innovation, Medical Devices | Johnson & Johnson
- **CHEN ADMATI** - Head of Intel Pharma Analytics Platform | Intel
- **DAPHNA MURVITZ** - Co-Founder & CEO | 8400 The Health Network
- **DAN SCHWARTZMAN** - CEO | MindUp
- **DANA GOUREVICH** - Director of CTO Unit | Israel Innovation Authority
- **EFRAT SHEFER** - GM, Imaging Clinical Applications & Platforms at Philips; President | Philips Israel
- **ESTI SHELLY** - Director of Digital Health Unit | Ministry of Health Israel
- **EYAL ZIMLICHMAN, MD** - Deputy Director, Chief Innovation Officer | Sheba Medical Center
- **GUY SHAULI** - Director, Global Digital Partnerships | AstraZeneca
- **HADAS BITRAN** - Principal Group Manager of the Health Group | Microsoft Israel R&D Center
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- **ISRAEL SHAMAY** - Senior Director of Americas Operations, International Collaborations Division | Israel Innovation Authority
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- **RUTH BERGMAN** - Director of Engineering at Acute Care | GE Healthcare
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- **TALOR SAX** - CEO | eHealth Ventures
- **TAMARA MANSFELD** - Global Innovation Lead | Pfizer
- **TERRY O'DWAYER** - Co-CEO and Co-Founder | LSX leaders
- **TOMER STAVITSKY** - Corporate development & M&A | Intuitive Surgical
- **Yael GLASSMAN** - CEO | Nutrino (Acquired by Medtronic)
- **YAIR SCHINDEL** - CEO | aMoon fund
- **SHAI-LEE SPIGELMAN** - CEO of Digital Israel | National Digital Bureau
- **TOMER EPSTEIN** - Head of Medical Device & Digital Health | Israel Export Institute
- **Yael OPHIR** - Executive Director | Digital Health - HealthIL
- **YARON ITZHARI** - Israel's Country Director | Medtronic

6. FOOTNOTES

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17. TASC analysis based on data from the Start-Up Nation Central Website. As part of the analysis we classified the startups according to the following areas: **Data-Analytics:** Decision support, Diagnostics | **mHealth:** Digital Therapeutics, Patient Engagement, Assistive Devices | **Telemedicine:** Remote Monitoring | **E.H.R:** Clinical Workflow

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The information included in this guide is relevant for February 2020. The content included is intended to provide only a general outline of the subjects covered and it is necessary that specific professional advice be sought before any action is taken.



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