HEALTHCARE & LIFE SCIENCES REVIEW

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TOO BIG TO IGNORE! PAGE 25

TURKEY NOVEMBER 2021
Acknowledgements

PharmaBoardroom is profoundly grateful to...

Burak Dağlıoğlu, president, Investment Office of the Presidency of the Republic of Turkey

Savaş Malkoc, secretary general, Pharmaceutical Manufacturers Association of Turkey (IEIS)

Dr Ümit Dereli, secretary general, Association of Research-Based Pharmaceutical Companies (AIFD)

Dr. Hamdi Akan, head of the executive board, Clinical Research Association

Dr. Erhan Akdoğan, president, Health Institutes of Turkey (TUSEB)

Dr Tolga Karakan, president, Turkish Medicines and Medical Devices Agency (TiTCK)

İsmail Yormaz, vice president and regional director South East, Recordati

Abidin Gülmüş, CEO, GEN

Dogan Taskent, board member, Swiss Chamber of Commerce

İbrahim Ethem Tokgözlu, Expert, Sectoral Activities Unit, Investment Office of the Presidency of the Republic of Turkey

for their continuous support, enthusiasm and encouragement in the compilation of this report.
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— November 2021

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The Healthcare & Life Sciences Review was produced by PharmaBoardroom.

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For exclusive interviews and more info, please log onto www.pharmaboardroom.com or write to media@pharmaboardroom.com

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Dear Readers,

The Turkish economy grew by an average of 5.1 percent between 2003 and 2020 thanks to the successful macroeconomic policies that were implemented, the reforms that were carried out uninterruptedly, and the political stability that was achieved under the leadership of President Erdoğan. In the same period, Turkey established itself as a center of investment in the region by attracting USD 225 billion of foreign direct investments (FDI).

The timely adoption of target-oriented measures against COVID-19 not only made Turkey’s fight against the pandemic more effective, but also ensured that its economy was relatively less affected. According to IMF, in 2020, Turkey recorded the second highest growth among G20 countries, becoming the world’s 11th largest economy in terms of purchasing power parity. In the first quarter of 2021, it maintained its position with a growth of seven percent: 56 percent of this growth rate resulted from net export and investments, which is an indicator of balanced and healthy growth.

In this context, the sustained economic growth and strong health industry in spite of the unforeseen conditions and crisis has proven the resilience of Turkey. Worldwide, FDI was among the areas adversely affected by the pandemic. According to the United Nations Conference on Trade and Development (UNCTAD) figures, global FDI dropped by 35 percent in 2020. Turkey attracted around USD 7.8 billion of FDI in 2020, reporting a nearly 15.5 percent decline.

Of course, the pandemic has reminded us of the importance of the life sciences sector and companies operating there. FDI plays a very important role in the progress made by the Turkish healthcare industry and research ecosystem today. Over 20 multinational pharmaceutical companies have made sizeable investments, improving the country’s medical technology ecosystem. With health expenditures exceeding USD 35 billion as of 2019, Turkey is a center that attracts the attention of the global health ecosystem, particularly pharmaceuticals and medical technologies. Our healthcare industry has leveled up thanks to the attractive investment opportunities we offer, contributing to the establishment of a modern ecosystem that meets international standards. Within this framework, the Presidency of The Investment Office are involved in these efforts by striving to bring new added-value and technology-intensive investments into the ecosystem and enhance the reliability of existing investments.

We believe that this 2021 edition of Healthcare and Life Sciences Review Turkey will highlight the investment opportunities in Turkey in the field of healthcare and life sciences, based on concrete examples. This report will fulfill a significant need in the healthcare sector, whose focus on research, science, technology, and innovation greatly impacts public health.

I would like to express my gratitude to all those who have contributed to the preparation of this issue, especially PharmaBoardroom, and all the relevant private sector representatives who have supported our endeavor to bring Turkey to the position it deserves in the international arena. I hope that this report will provide readers with answers to their questions regarding the healthcare industry and investment environment in Turkey.

A. Burak Dağlıoğlu
President
Presidency of the Republic of Turkey Investment Office
Distinguished members of the international healthcare community,

As the Chairman of the Pharmaceutical Manufacturers Association of Turkey (IEIS), I am very pleased to reach out to you through this comprehensive report that highlights the investments that have been made into the Turkish pharmaceutical industry, the country's rising R&D competence, its high production levels, and its export capacity.

The COVID-19 pandemic has reinforced the fact that a strong healthcare system and pharmaceutical industry is vital for all countries. Turkey’s strong and self-reliant pharmaceutical industry has been of crucial importance since the outbreak of the pandemic, continuing production without interruption despite difficulties ranging from the supply of raw material to logistics disruptions, increasing costs, fluctuations in pharmaceutical sales, and the challenging circumstances created by the risk of contagion. Through these means our country’s supply safety was able to be maintained, and our people and healthcare professionals faced no problems in accessing pharmaceuticals.

Around 680 organizations are operating in our industry, with 33 accredited R&D centers, 99 pharmaceutical and 11 raw material production facilities meeting the highest international standards. With over 40 thousand highly skilled employees, the pharmaceutical industry provides over 12 thousand products. Locally produced products currently make up 88 percent of the market in terms of volume.

Our association aims to transforming the Turkish pharmaceutical industry into a leading producer and exporter, producing higher value-added products particularly in the biotechnology field by enhancing R&D proficiency.

We feel that the support mechanisms of the government, along with our efforts, are extremely important for the improvement of the industry, and we gladly keep track of the steps taken in this regard.

Evidently, biopharmaceuticals are shaping the present and future of the global pharmaceutical industry. Thus, in the last 5 years, our industry has made very impressive investments in this field. The amount of investment incentive certificates received by our companies over this period has reached USD 1.1 billion. In addition, intensive technology transfer, know-how, and human resources investments are made for these products. Moreover, we continue our investments abroad and establish strategic partnerships with the world’s leading biotechnology companies.

For Turkey to compete effectively with its competitors and be successful in this field, a supportive ecosystem needs to be established. Enhanced licensing regulation that will shorten time-to-market is crucial. Besides, new incentive schemes geared towards more public funding are of utmost importance.

Lastly, I would also like to mention our industry’s strong exports performance. In the last three years, our pharmaceutical export has increased above Turkey’s average. As for the end of 2020, our export has increased of 27.3 percent and reached a record-breaking level of US 1.84 billion. We export to nearly 180 destinations including the European Union, Commonwealth of Independent States, North Africa, and the Middle East.

As the Pharmaceutical Manufacturers Association of Turkey, we will continue to pursue our passionate and dedicated efforts to render our industry as a global actor with a vision centered around R&D and biotechnology, manufacturing, employment, and exports.

Nezih Barut
Chairman
Pharmaceutical Manufacturers Association of Turkey (IEIS)
On the verge of its 100th anniversary, the Republic of Turkey appears to be approaching a decisive moment in the trajectory of its healthcare industry. With a comprehensive social security system covering over 95 percent of the population already in the bag, and after more than a decade of investment on world-class infrastructure, the country now seems willing to take the next step, striving to consolidate a globally competitive local industry.

The era of booming profits for the pharma industry is in the rear-view mirror, but new opportunities have arisen for companies willing to align with the country’s ambitious Vision. It is, after all, the 18th largest market in the world, worth over USD seven billion per year.

As the local industry races to the front of the upcoming biosimilars bonanza and pivots toward exports, multinational innovators are increasingly betting on clinical trials and new generation treatments as an ever-greater proportion of their value proposition.

Localization has consolidated Turkey’s manufacturing base and investment has continued to pour in, with patients reaping the benefits. The COVID-19 pandemic threatened to set the whole system back, but it left an invaluable learning instead, that selfless collaboration can lead to greater innovation.

Through the exclusive insights of policymakers, key opinion leaders, heads of local pharma and medtech companies, as well as multinational affiliate leaders, the story of a country in a make-or-break moment has emerged.
We speak directly with healthcare leaders and pharmaceutical executives globally.
SNAPSHOT IN FIGURES

Macroeconomy

TURKEY SNAPSHOT

Source: World Health Organization, Turkey Statistical Institute, The World Bank

Population 83.6 million (18th largest in world)

Total Area 783.562 km2 (38th largest in world)

Life Expectancy at Birth 74.4 years (39th highest in world)

GDP USD 720 billion (2020) (13th highest in world)

GDP per capita (PPP) USD 28,120 (2020) (57th highest in world)

GDP (USD BILLIONS) 2011-2020

Source: The World Bank

838.7 880.5 957.7 938.9 864.3 869.6 858.9 778.3 761.4 720.1

POPULATION PYRAMID

Female TURKEY Male

Female EUROPE Male
BRIEF HISTORY OF THE TURKISH PHARMA INDUSTRY

1948-1952 Pharmaceutical manufacturing facilities

1928 Pharmaceutical Medical Preparations IAW no. 1262

1984 Introduction of GMP, many other GxP

2004 New pricing system based on reference pricing. Health transformation program

2008 Accession to PIC/S membership

2020 Membership to ICH

VALUE OF THE TURKISH PHARMA MARKET

<table>
<thead>
<tr>
<th>Year</th>
<th>Value (TRY Billion)</th>
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<tbody>
<tr>
<td>2010</td>
<td>13.4</td>
</tr>
<tr>
<td>2011</td>
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<td>2012</td>
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<tr>
<td>2013</td>
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<td>2018</td>
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<tr>
<td>2019</td>
<td>40.7</td>
</tr>
<tr>
<td>2020</td>
<td>47.9</td>
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ORIGINATOR-GENERIC DRUGS BY VALUE

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<th>Reference (TRY Billion)</th>
<th>Equivalent (TRY Billion)</th>
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<td>5.4</td>
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<tr>
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<tr>
<td>2017</td>
<td>16.7</td>
<td>7.9</td>
</tr>
<tr>
<td>2018</td>
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<tr>
<td>2019</td>
<td>27.0</td>
<td>13.7</td>
</tr>
<tr>
<td>2020</td>
<td>32.7</td>
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</table>

BIOPHARMACEUTICALS MARKET

<table>
<thead>
<tr>
<th>Year</th>
<th>Reference (M Boxes)</th>
<th>Biosimilars (M Boxes)</th>
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<tr>
<td>2010</td>
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<tr>
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<tr>
<td>2020</td>
<td>11.0</td>
<td>32.0</td>
</tr>
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</table>

% SHARE BY THERAPEUTIC AREAS

- Oncology: 38%
- Antidiabetes: 17%
- Digestive System: 6%
- Others: 25%
- Blood Derivates: 15%

Biosimilars’ share in total biopharma market
SNAPSHOT IN FIGURES
Manufacturing

MANUFACTURING BASIC FACTS

85
Number of Pharmaceutical Production Facilities Approved by TİTCK

USD 1.8 b
Volume of Turkish pharmaceutical exports in 2020.

23
Among the 94 manufacturing facilities, 23 are owned by multinational companies.

170
Turkish pharmaceutical manufacturers are exporting to more than 170 countries, including the EU, MENA, and CIS countries.

PHARMACEUTICAL EXPORTS (2017 VS 2020)

Source: UN Comtrade HS Code 30

(USD MILLIONS)


421 558 662 995 1,310 1,430 1,826

Growing by 84% in 3 years

LABOR COST PER HOUR IN MANUFACTURING

Source: Eurostat, OECD

($, 2018)

Germany France USA UK

47.2 44.4 39.6 31.1

Czech Republic Slovakia Hungary Poland Romania Bulgaria Turkey

14.9 14.3 11.5 10.7 7.0 5.6

UNDERGRADUATE AND GRADUATE ENROLLMENT IN RELATED FIELDS (2020)

Source: Ministry of National Education, Council of Higher Education, Turkstat

TOTAL 187K

Biochemistry Pharmacy

Chemistry Biology Medicine

Source: Eurostat, OECD
SNAPSHOT IN FIGURES

R&D

NUMBER OF PATENT APPLICATION IN SECTORAL FIELDS IN THE LAST 10 YEARS

<table>
<thead>
<tr>
<th>Year</th>
<th>Medical Technologies</th>
<th>Vaccines and Drugs</th>
<th>Biotechnology</th>
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<td>283</td>
<td>21</td>
</tr>
<tr>
<td>2020</td>
<td>517</td>
<td>150</td>
<td>9</td>
</tr>
</tbody>
</table>

Source: Sistem Global, Invest in Turkey

COMPANIES/INSTITUTIONS WHICH MADE THE MOST PATENT APPLICATIONS IN THE PHARMACEUTICAL SECTOR

<table>
<thead>
<tr>
<th>Institution</th>
<th>Medical Technologies</th>
<th>Vaccines and Drugs</th>
<th>Biotechnology</th>
</tr>
</thead>
<tbody>
<tr>
<td>SANOVEL İLAÇ SAN. VE TİC. A.Ş.</td>
<td>968</td>
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<td>BİLGİC MAHMUT</td>
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<td>ARVEN İLAÇ SAN. VE TİCARET A.Ş.</td>
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<td>290</td>
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<td>ERDAL CAN ALKOCLAR</td>
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<td>SIMA PATENT VE LISANSLAMA HİZ. LTD. ŞTİ</td>
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<td>MONTERO GIDA SAN. VE TİC. A.Ş.</td>
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<td>DEGUSSA</td>
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<tr>
<td>T.C. İSTANBUL MEDÜPOL ÜNİVERSİTESİ</td>
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<td>RADOPATH PHARMACEUTICALS INTERNATIONAL LTD.</td>
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<td>50</td>
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Source: Sistem Global, Invest in Turkey
MINISTERIAL PRIORITIES

Overseeing healthcare for a population of over 80 million, Turkey’s Ministry of Health was put under the spotlight during the COVID-19 pandemic. Here, we highlight four of the hot-button items on Minister of Health Dr Fahrettin Koca’s plate as Turkey emerges from the pandemic period.

Pandemic Learnings
A few months after WHO Director-General Tedros Ghebreyesus, described Turkey a strong healthcare champion of 2021 during a virtual press conference, Minister Koca pointed to the injustices in access to healthcare as one of the main learnings from the pandemic during a G20 meeting.

The Minister, who oversees Turkey’s public healthcare system, called for a renewed long-term vision that includes achieving universal health coverage as the main goal of health-related Sustainable Development Goals. Unlike some other countries, Dr Koca said, Turkey’s healthcare system was not unprepared for the pandemic, pointing to the publication of the Pandemic Influenza National Preparedness Plan in 2019.

2021 Budget
When Minister Koca presented the 2021 budget of the Ministry of Health at the Turkish Parliament’s Planning and Budget Commission at the end of 2020, he stressed that the pandemic was and would continue to be their primary agenda, and that his department would continue fighting for a country where “the whole society adopted a healthy lifestyle and everyone’s right to health was safeguarded.”

However, with one of the highest diabetes rates in Europe and an obesity rate of 34 percent, Dr Koca also underlined the importance of fighting chronic. “Our goal is to increase the number of obesity centers to 140 in 2021,” he stated.

Finally, he explained his plan to increase the efficiency of the system by strengthening “family practice to make sure that we reduce unnecessary consultation to secondary and tertiary healthcare services.”

Vaccine IP
“It is unfortunate that a solution has yet to be found,” said Dr Koca during an international forum on vaccine cooperation in August, referring to the stalemate regarding the limits of intellectual property rights during the pandemic. “This situation reveals the inadequacy of past mechanisms and the need to take firm steps towards the future as soon as possible.”

“The process has clearly demonstrated to us the need for international cooperation on matters such as scaling up of R&D efforts, funding support, information-sharing, vaccine production capacities, technology transfer, distribution capacities, emergency use listings, using and sharing data, pricing policies, and fighting vaccine hesitancy and misinformation,” he added.

Trying to lead by example, the minister noted that Turkey had 20 vaccine studies registered with the WHO and that the country would make their vaccines available to “the whole world” once clinical studies were completed. “Access to vaccines is a health right that everyone should enjoy.”

Protecting the Frontline
Through an editorial co-authored with the director of the WHO health workforce, Dr Koca put the spotlight on the challenges faced by frontline healthcare workers during the pandemic.

“[Frontline workers] faced accelerated rates of infection and deaths, lack of adequate personal protective equipment, social discrimination and attacks, and the dilemma of working in COVID-19 settings and returning home to care for friends and family members,” read the editorial.

Following the solidarity approach to domestic vaccines, the minister explained that while access to personal protective equipment was prioritised for domestic use, but “out of international solidarity, Turkey also sent protective and medical equipment to 156 countries and nine international organisations.”
What are TITCK’s main competencies and what role does it seek as Turkey’s medicine regulator?

**TOLGA KARAKAN (TK):** The agency aims to carry out regulatory, supervisory, and guiding activities entrusted with legal and administrative regulations and high-policy documents regarding the production, supply to the market, and consumption of pharmaceuticals, medical devices, traditional herbal, supportive and advanced treatment medicinal products and cosmetic products. I continue to contribute to the agency’s efforts to become a people-oriented, scientifically based, value-producing, internationally leading reference agency during my term in the office. The agency significantly contributes to Turkey’s competitive position in the international market.

TICK is involved with international platforms such as the European Union Commission working groups, Pharmaceutical Inspection Co-operation Scheme (PIC/S) and is a member of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) that aims to harmonise worldwide regulations to ensure that medicines are effective, safe and of high quality.

TITCK has joined the ICH, verifying that Turkey meets international standards for regulatory aspects of medicines. What are you expecting to leverage from this?

**TK:** TITCK was accepted as a member of the ICH on 27 May 2020, an organization that aims to harmonize worldwide regulations to ensure that medicines are effective, safe and of high quality.

ICH membership indicates TITCK’s and sector’s commitment to the highest global standards for quality, efficacy and safety in pharmaceuticals. In addition, this membership has enabled TITCK to have a worldwide voice in the field of pharmaceuticals and has made it one of the countries that will determine the rules in this regard. ICH membership reinforces the confidence in Turkey in terms of the pharmaceutical industry and reveals the quality of TITCK’s evaluation processes. This supports both the foreign industry’s investment in the country and the domestic industry’s exports.

Turkey’s Vision 2023 is focused on global competitiveness for the pharma and biopharma industry. A good level of regulatory science is a critical point, especially in the nurturing and development of clinical trials. What role will TITCK play in incentivizing clinical trials?

**TK:** Turkey’s ambition is to increase its competitiveness in the global pharmaceutical market and to occupy a higher position in the value chain. In line with this policy, we are aiming to be a regional leader in clinical trials; the country aims to increase its share from global clinical trials both in numbers and economically. In this context, Turkey has taken several initiatives in recent years, including the legal regulations it has implemented to improve the clinical trial environment and, with a solid legislative infrastructure that follows EU standards, it has become a strong candidate for multinational clinical trials.

For its part, TITCK has made great progress in recent years in terms of structural changes and improvements and evaluation times. While the average application evaluation period was 100 days in 2016, this period decreased to 26 days in 2020. 🌟
Shifting Priorities: Clinical Trials, Biologics, R&D Investment

There are perhaps no two words that better summarize the last few years in Turkish pharma than localization and pricing. But after years of investment and struggles, the country’s priorities appear to be shifting.

Turkey’s Vision 2023, as defined in its 11th Development Plan, has changed the government’s vision regarding pharmaceuticals as it looks to make the industry competitive at a global level. To coincide with the nation’s 100th anniversary, the goal has been set of becoming a top ten economy in health services by 2023.

“This ambitious goal differs greatly from the former objective of becoming a manufacturing hub to supply domestic demand,” says Ümit Dereli, secretary general of the Turkish Association of Research-Based Pharmaceutical Companies (AİFD), which has 35 multinational member companies that together account for almost 50 percent of the Turkish market. “The pandemic reinforced the importance of manufacturing, but we need to think beyond the local market and move towards exports. There is a new understanding of the pharma industry in Turkey and the value it can bring; the perception is not as limited as before.”

The priorities outlined by Dereli’s counterpart at the Turkey’s Pharmaceutical Manufacturers Association (IEIS), Savaş Malkoc, seem to fit within the new scheme since IEIS is working to increase “export capacity and the competitiveness” of the Turkish pharma industry.

Both associations, however, are taking differentiated approaches.

For AİFD, representative of multinational innovators, a critical element is becoming a regional leader in clinical trials. “These areas have an economic value, but also expand a country’s capabilities and make it a stronger part of global networks. Additionally, clinical trials can bring early access to innovation for unmet clinical needs,” argues Dereli.

According to Dereli, almost all industry-supported clinical trials conducted in Turkey...
There is a new understanding of the pharma industry in Turkey and the value it can bring

Ümit Dereli  AIFD

are led by AIFD member companies, most of them in oncology and rare diseases. Turkey currently has sufficient infrastructure to host studies from Phase I to phase III.

If the country is to achieve global competitiveness, Dereli contends, TITCK must be a globally respected regulatory authority and, fortunately, the country is moving in that direction, looking at Swissmedic, FDA, EMA and others as an example. As evidence, he describes TITCK becoming a member of PIC/S and ICH as “the most important development regarding the sector in recent years.”

For IEIS, representative of domestic manufacturers, biologics are a top priority, categorizing them as the “present and future of the global pharma industry.” In 2020, biologic products reached a market share of 25 percent in Turkey. “It is unthinkable for us to lag behind the biotech transformation considering our deep-rooted and powerful pharmaceutical industry, which has a history of more than a century. However, in the current situation, we see that our country is still largely dependent on foreign sources in this product category,” says Savaş Malkoc, although adding that “impressive” investments have been made in the field in the last 5 years.

“The amount of investment incentive certificates received by our companies in the recent period has reached USD 1.1 billion. In addition, intensive technology transfer, know-how and human resources investments are being made for these products,” he reveals, “enhanced licensing regulation that will shorten time-to-market is of utmost importance. New incentive schemes geared towards more public funding would be of help. Patients should be encouraged to begin treatment with biosimilars produced in our country.” At the moment, 29 biosimilars under 7 different brands are available in the country.

Common goal: R&D support

AIFD members’ main contribution to R&D is currently coming from investment in clinical trials inside the country, but the association has taken on the mission of fostering homegrown innovation, particularly from startup companies. That is why they are running the BIO Start-up program, “the first and only” life sciences and biotechnology accelerator program in Turkey, according to Dereli.

“We receive around 50-60 applications every year, out of which 15-20 start-ups are admitted to the program based on their competence in terms of team quality, business idea and the maturity stage like proof of concept,” he explains. A jury then selects 5 start-ups to participate in the BIO Convention, the world’s largest biotechnology event, organized in the US. “Hopefully, those start-ups will become the next success stories from Turkey... the future of innovation in pharmaceuticals cannot be limited to certain geographies, innovation is everywhere, and we cannot afford to miss out on any opportunity.”

When it comes to IEIS and local manufacturers, the focus is on R&D investment to produce value added products. “We are producing mostly generics which are not generally associated with high technology. There is a gap between the reality and perception of the Turkish pharma industry abroad. We have EMA-certified facilities that can even produce biologic products, including mRNA vaccines,” says Savaş Malkoc.

In general, Big Pharma companies spend around 15 percent of their revenues in R&D, but in Turkey the number remains around 5 percent, something that Malkoc recognizes: “All of our members are aware that the number must be increased substantially. At the same time, we believe that government policies should be re-organized drastically to accommodate more R&D spending and change the current pricing and reimbursement system.”
The responsibility for coordinating Turkey’s research and development effort to produce its own COVID-19 vaccines and drugs fell on two main public agencies: the Health Institutes of Turkey (TUSEB) under the Ministry of Health and the Scientific and Technological Research Council of Turkey (TÜBİTAK), under the Ministry of Industry and Technology. National regulatory body TITCK began preparing guidelines in consultation with the WHO back in March 2020 with detailed information to guide the research groups that would conduct COVID-19 vaccine studies.

“We decided to support several projects, and, in hindsight, it was the right decision. We have discovered a new collaborative model where researchers, companies that produce...
vaccines, and academicians can work together inside vaccine factories,” explains TUSEB’s president, Erhan Akdoğan. One of the vaccine candidates supported by the agency is currently in phase III clinical trials.

On the other side of the effort, TÜBİTAK brought the ecosystem’s drug and vaccine development competencies under a unified “COVID-19 Turkey Platform,” counting 436 researchers from 49 different institutions to work on 17 projects, seven of which were vaccines.

“Co-creation based approaches are transforming the way R&D and innovation is being conducted with interactive processes replacing linear processes,” contends Dr. Hasan Mandal, president of TÜBİTAK.

The model described by both Akdoğan and Dr. Mandal began with an initial funding of just around USD 200,000, which proved to be relatively sufficient due to one factor, selfless collaboration.

Projects were able to progress, according to multiple industry stakeholders, because academics did not charge a dime for their work – using funds to buy material only. universities opened their laboratories and companies provided their GMP production facilities and R&D labs for free, without purchase guarantees from the government.

“Collaboration was critical... It was a miracle. It proved that people can come together for the greater good. Other countries were able to throw money at the problem, but that was not the case for us,” explains Dogan Taskent, board member of the Swiss Chamber of Commerce in Turkey.

This opinion is shared by TUSEB’s Akdoğan, “these initiatives developed rapidly with the help of the laudable efforts from scientists, the pharmaceutical industry and universities. The priority given by the Minister of Health for vaccine production has played an important role in accelerating the process.”

Progress made

Apart from the discovery of the advantages of a collaborative approach to R&D, Turkey’s effort is providing tangible results.

As of the writing of this report (October 2021), one candidate is ongoing phase III clinical trials in the country with 40,000 participants, Turkovac, an inactive vaccine jointly developed by the MoH, TUSEB and Erciyes University.

On the competing side, TÜBİTAK’s most advanced project, a virus-like particle (VLP) vaccine candidate became the first to enter clinical trials and just the fourth VLP to do so globally. Confident about the potential of the vaccine, Dr. Hasan Mandal and Dr. Faruk Özlü, Minister of Industry and Technology, volunteered for the initial studies. The candidate is expected to begin phase III trials.

Beyond vaccines, the COVID-19 Turkey Platform includes 10 different treatment-oriented drug development projects that involve drug molecular modelling, recombinant neutralizing antibody, convalescent plasma and synthetic drug synthesis and production.

“Co-creation based approaches are transforming the way R&D and innovation is being conducted with interactive processes replacing linear processes.”

Dr. Hasan Mandal  TÜBİTAK
The number of pharma production facilities in the country went up by almost a third from 2015 to 2020, and production of pharmaceutical products increased 52 percent in that period, according to TurkStat and the Pharmaceutical Manufacturers Association of Turkey (IEIS).

In fact, 2020 was a record-breaking year after pharma exports reached USD 1.84 billion. Becoming one of the world’s leading pharmaceutical producers and exporters is one of the main objectives of the Turkish industry, according to the most recent IEIS report.

“I believe that the domestic price pressure has been driving companies to sell products abroad; that is why medicine exports have consistently increased over the past five years. There is a huge gap between the prices you get abroad for medicines from the ones you get in Turkey because the government uses a special exchange rate... I foresee this trend, of companies manufacturing in Turkey for foreign markets, will continue in the next years,” explains Savas Malkoc, secretary general of IEIS.

The low prices referenced by Malkoc translate into low margins for manufacturers in an already crowded market. As a result, Turkish players have been forced to look elsewhere for profits.

“It helps that Turkey is a strong market with a sizeable population that enjoys almost universal healthcare coverage, but the pricing system is a difficult challenge for the industry... We believe that the Turkish market will not continue growing due to the low profit margin; that is the reason we are looking for opportunities abroad,” asserts Ufuk Kumrulu, chairman of Polifarma, a leader in parenteral solutions that generated 32...
percent of its sales in export markets in 2020. “Exports are crucial for the company’s future and ambitions,” he says.

The situation is not so different for DEVA, a 63-year-old company acquired by Swiss investors in 2006. International markets were a big part of the strategy when the new ownership took charge, according to its current CEO and chairman of the board, Philipp Haas, “the new manufacturing facilities, from both a quality and capacity point of view, were built with the objective of exporting into high-quality developed markets. It will help us maintain our great quality but at lower costs.”

The company has a direct presence in the United States, Germany, Switzerland and a few other markets, and believes that its strategy is aligned with Turkey’s since the country is looking to reduce the pharma trade deficit.

In the first quarter of 2021, President Erdoğan announced a new innovative reform package focusing on the economy and legal system. That reform package included policy changes to increase Turkey’s participation in global value chains, explains Burak Dağlıoğlu, president of the Presidency’s Investment Office, “we, as a country, follow, attach importance to, and support the life sciences industry with all our relevant institutions.”

Where to go?

Being capable of manufacturing a wide range of quality products is only one part of the value proposition from Turkish pharma manufacturers. There is also the unique geographical location of the country, at the crossroads between Asia and Europe, and the relative cost of manufacturing. According to 2018 data from Eurostat and the OECD, the labor cost per hour in manufacturing was USD 5.6 in Turkey, almost ten times lower than Germany and lower than competitors such as Romania, Poland, or Bulgaria.

As the general manager for Novartis in the country, Avinash Potnis, puts it, Turkey has a unique value proposition, offering “European perfection at an affordable cost.”

This assessment is shared by Dogan Taskent, board member of the Swiss Chamber of Commerce and R&D head for local manufacturer Atabay: “The Turkish pharma industry is highly regulated and follows international GMP, ICH and PIC/S standards. That means that Turkish pharma manufacturing is world-class in terms of quality but less expensive. Nearshoring is another advantage since the country is close to Europe and the MENA region.”

The big dilemma for companies is where to go. Different companies have taken different approaches that match their product category.

Last year, Turkish-made pharma products were exported to 177 countries, primarily to the European Union (EU), the Commonwealth of Independent States (CIS), North Africa and Middle Eastern countries (MENA); Asia was the biggest export region and South Korea the leading market with a whopping 33 percent of total exports valued at USD 616 million.

GEN, a manufacturer of complex generics and orphan drug distributor, opened an office in Russia in 2020 and another in Uzbekistan to support their presence in Azerbaijan and Kazakhstan. “We are leveraging Turkey’s historical ties and advantageous geographical location to strengthen our presence in CIS countries, but, since our objective is to be a major global company, we are also targeting Europe,” says CEO Abidin Gulmus.

Turkey’s market leader and largest pharma company, Abdi Ibrahim, is also emphasizing the importance of exports markets since close
to a fifth of their revenues are generated in the 60 countries they export to, including Canada, Europe, South Korea and the Middle East.

But, unlike most Turkish competitors, Abdi has manufacturing operations abroad (Algeria and Kazakhstan) and is planning to open affiliates in Germany and Saudi Arabia. “Internationalization is not an option, it is a path we must take because of the limitations in the Turkish market,” says CEO Süha Taşpolatoğlu, warning, however, that none of it will be possible without continued local success, “since Turkey is our main source of revenue, we must continue leading the market if we are to expand abroad.”

“Since Turkey is our main source of revenue, we must continue leading the market if we are to expand abroad.”

Süha Taşpolatoğlu ABDI IBRAHIM

WHERE TURKISH MANUFACTURERS ARE EXPORTING, PARTNERING, OR HAVE OPENED AFFILIATES
From Niche Distributor to Public Company

Few Turkish companies are experiencing such a transformational moment as GEN. In 2021 alone, the Ankara-based organization made its public debut on the Istanbul Stock Exchange and signed an exclusive collaboration agreement with Dutch biotech Sulfateq BV for the development and commercialization of a therapy against Alzheimer’s and other neurodegenerative diseases.

Leading GEN is Abidin Gulmus, a Turkish entrepreneur that started his first company, Pharmacia Diagnostics, in 1988. Pharmacia was initially focused on the laboratory diagnostics sector before expanding to the pharma industry via a partnership with Serono (now part of Merck KGaA).

After that journey, in 1998, Gulmus founded GEN “as a clean slate” to continue leveraging his expertise in the pharmaceutical field. However, aware of Turkish pharma industry dynamics, he opted to compete in a less crowded but complex niche: orphan drugs.

The company chose orphan drugs since other areas of the Turkish pharmaceutical market were “already saturated with me-too products,” says Gulmus. It was the start of a decades-long distribution partnership with Biogen, but other current partners include Ipsen, Jazz, PTC and Biomarin. “GEN is the first door knocked by the majority of companies working in the rare diseases space that does not have a direct presence in Turkey,” he adds.

Today, orphan drug partnerships remain the most lucrative business for GEN, perhaps because many companies are unwilling to register their products in Turkey, concerned that low prices could have a ripple effect on other markets. Despite the burdensome pricing system, Turkey’s legislation allows products to be introduced through a named-patient access program if a drug is not available in the market and addresses an unmet medical need, a right recognized by the Constitution of the Republic. That is why Gulmus calls Turkey’s social security system “one of the best and most humanitarian in the world.”

Orphan drugs opened the door for GEN, but the company had to expand its capabilities en route to its IPO. In 2018, on its 20th anniversary, GEN opened a manufacturing plant to produce complex generics. “We do not want to compete in a very crowded spaces, producing billions of tablets. Our objective is to produce high-cost, low-volume drugs that serve patients with unmet medical needs,” Gulmus contends, adding that the current objective is to export 70 percent of production in the next three years.

In line with their expansion strategy, GEN opened an office in Russia in early 2020 and acquired an R&D laboratory located in Hacettepe University Technopark in Ankara.

With the lucrative orphan drug partnerships and complex generics production businesses ongoing, the next step – one that Gulmus expects will propel the company to the next level – is developing and commercializing a new molecule. In this direction, GEN recently signed an exclusive agreement with Sulfateq BV, an early-stage Dutch biotech, for the development and commercialization of a therapy against Alzheimer’s Disease.

Referring to the project, Gulmus argues that an “effective treatment for Alzheimer’s Disease and other neurodegenerative diseases has been elusive, yes, but we must continue searching for it. This project’s upside is massive, we are talking about a potentially big reward for humanity.”
Can you begin by introducing the Toksöz Group, owner of Arven Pharmaceuticals, its presence in the Turkish market, and the role of Arven for the larger organization?

ZAFER TOKSÖZ (ZT): The Toksöz Group is a group of three companies, not a holding structure, which encompasses three different organizations: Arven Pharmaceuticals, Verano Pharmaceuticals and Montero. In addition, the Group currently owns 35 percent of Sanovel Pharmaceuticals, a manufacturer of generic medicines, after selling shares to a venture capital fund last year.

Arven Pharmaceuticals is the growth driver of the Group, whose primary focus is development and production of high-technology inhaler and biotechnology products.

Arven succeeded in developing the patented and produced dry powder inhaler DPI in Turkey, Arvohaler, as a result of long-lasting R&D activities. That product is not exactly a generic; in the United States it qualifies for the 505(b)(2) drug approval pathway, registered as a semi-original product because the drug delivery system is different.

Arven’s main expertise is research and development, so we choose products that are difficult to produce as evidence by the fact that we are one of only 15 companies in the world competing in the DPI sector. While the company excels in R&D and manufacturing, it is lacking global commercialization capabilities.

Arven is also known as the company behind the first biosimilar drug, developed and manufactured from cell to final product in Turkey. Can you explain your presence in the biosimilar space?

ZT: Arven owns a production facility for two different types of biosimilar products: monoclonal antibodies predominantly produced in mammalian cell culture bioprocesses, and bacteria based biosimilars.

In 2016, the company obtained marketing authorization for the biosimilar of Neupogen (filgrastim), marketed under Fraven, which is the first biosimilar drug, developed and manufactured from cell to final product in Turkey. Filgrastim is used by almost every oncological patient going through chemotherapy and we are the market leaders in Turkey for that biosimilar. For this product, we have been able to increase the efficiency of the cell by ten times.

Our advantage is due to unparalleled investment in biosimilar R&D and production; no other company in Turkey has invested as much as Arven. The main challenge in biosimilar production is the know-how, which is what we have been doing for the last 15 years.

Today, Arven’s team is capable of developing from cell line, called upstream, to industrialization, what the industry calls scale up. Many of the Turkish companies with investments
in biosimilars have not looked at the strategic value of the overall process but rather at the fill and finish side only. The technological infrastructure required for biosimilars is also used for recombinant DNA vaccines, for example, which is why Arven invested on the new injectable lines for high-scale products this year.

With an already successful business for your DPI products, what is your strategy moving forward to become a leader in biosimilars?

ZT: Arven is currently a small-scale company, not a big scale one; financially, we have to adapt our investment in accordance with the Turkish market’s reality.

Two years ago, we invested in trastuzumab and bevacizumab, two monoclonal antibodies, which were ready for the scale up process and first clinical studies, but unfortunately the reimbursement system in Turkey made prices for those products too low for us to consider it a feasible investment.

The government is buying most of these products through tenders and a low pricing strategy. The issue is that companies that own the originator product see Turkey as 1 percent of the global market and can sometimes sell it at cost, with extremely low margins or none at all. But Turkey is 100 percent of the market for Arven.

We tried to explain to the authorities in Ankara that such low prices would make it hard for us to sell them in Turkey since clinical trials would have cost too much. The alternative is selling them abroad but globalizing one biosimilar product requires USD 30-40 million investment for clinical studies.

For this reason, we have decided to stop our own development of biosimilars, changing our strategy in order to become a CDMO, offering our capabilities to develop and manufacture for other companies.

Our strategy is to offer our unique set of biosimilars capabilities to any organization that wants to enter the business but does not have its own manufacturing or development know-how in Turkey. The investment in new sterile injection lines that I mentioned allows Arven to offer a full package for companies in search of a CDMO.

This is a great opportunity today since many global CDMOs are running at capacity with pandemic-related projects, and because Turkey remains a very cost-effective country to manufacture. We are also looking for a strategic partner that can carry our company to international platforms.

Turkey’s Scientific and Technological Research Council’s (TÜBİTAK) president, Hasan Mandal, explained that they funded 35 healthcare projects during the pandemic. Is Arven currently collaborating with them or other public institutions?

ZT: Both TUSEB and TUBITAK are very friendly and helpful, always trying to support and invest in different projects, but their budget is limited. Creating one monoclonal antibody cannot be done with USD 500,000, it is not possible because you need to invest millions in clinical studies. In addition, both institutions are currently concentrated on the vaccine projects.

Can you tell us about your background and how you got involved with the biopharma industry?

ZT: I studied chemical engineering at Boğaziçi University in Turkey and did a two-year MBA afterward. My father was a well-known pharmacist and founder of Sanovel, and I worked with in the pharmaceutical sector until he passed away in 2012. I have always been involved in the R&D part because of my passion towards solving difficult problems.

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Too Big to Ignore!

Recent years have certainly been a wild ride for the Turkish life science industry. On the one hand, pharma executives have found themselves navigating repeated currency crises, an unorthodox pricing system and the fallout from the global pandemic. On the other, they have basked in the glow of a welter of highly impactful state interventions intricately designed to supercharge exports, increase medicine coverage, and unleash unprecedented levels of innovation.

Indeed, today’s Turkish pharma landscape is a colourful melting pot of contradictions. A country that has both gained global kudos through its admission into the international PIC(s) alliance of pharmaceutical jurisdictions yet provoke the ire of the EU for pursuing a controversial localization policy. A marketplace renowned for being the most mature in its region, but increasingly host to a bubbling and evermore vibrant biotech sector. A standout national healthcare system that is the envy of its neighbours, though one where the public health envelope still accounts for a meagre 4.5 percent of GDP.
Meanwhile the Erdogan administration’s grand ambition of rendering Turkey a top ten pharma hub in time for the Turkish Republic’s centenary in just over a year’s time looms large over a life science industry that appears to be picking up pace again. Bucking expectations, Turkey’s pharma market breached the 48 billion TL mark (USD 8 billion) in 2020 – registering a 17.7 percent increase on the year before and becoming the world’s 18th biggest pharma market in the process with a 1.5 percent slice of global market share.

For sure, the local pharma market outlook shines bright. With the nation currently registering the second-highest GDP growth among G20 countries and managing to maintain a rate of seven percent well into 2021, many are expecting the proceeds of growth to spill over into the life science space. “The excitement is back,” confides Ingrid Drechsel, pharma cluster division head for Turkey & Iran at Bayer. “The fact that we are now consistently outstripping European growth averages again is welcome news and suggests Turkey will soon be able to carve out a bigger role in international pharma: IQVIA short-term projections already predict us rising up the rankings to claim 14th spot.”

Besides, prolonged double-digit growth for the pharma industry looks very much on the cards given the unique socio-demographic characteristics underpinning Turkey’s 85 million-strong population. “Without doubt this is a place with tremendous untapped growth potential. Aside from the sheer size of the patient pool, you’ve got an extremely high prevalence of chronic disease juxtaposed with better diagnosis and disease awareness, a strong commitment at a policy level to guarantee comprehensive and universal healthcare coverage, and an ageing population whereby ten percent of Turks will soon be over the age of 65,” exclaims Evren Özlu general manager for Turkey and Sub-Saharan Africa at Boehringer Ingelheim. “This is a marketplace where there’s both a lot of work to be done, and where the conditions exist to be able to actually do it.”

“The mood is increasingly upbeat,” agrees Burak Dağlioğlu, president of the Investment Office of the Presidency of the Republic. “Turkey is positively differentiated from the other emerging markets, especially in the life sciences sector, thanks to a resilience that has been demonstrated time and time again, a very strong demand curve and the legacy of astute investments over the past decade that are now beginning to bear fruit.”

For him, it’s also a juncture where the Turkish life science industry can really seize the initiative and start showing off its true potential. “I think there’s a growing realization that we have a great deal to offer in times like this. For example, recent analysis by the credit rating agency Fitch, names us as an excellent destination for relocating investors – in other words an ideal location for multinationals looking to diversify their supply chains at a moment when much of the rest of the world remains in flux in the aftermath of COVID-19,” he ventures.

Certainly, there has been no lack of foreign direct investment into the Turkish pharma and medtech sectors in recent years. In the last 15 years alone, the Turkish life science space has received over USD 725 million worth of FDI including 40 greenfield infrastructure projects, with internationally renowned drug developers such as Novartis, Sanofi, Novo Nordisk and Recordati, alongside big-brand medical device players such as Medtronic and Hitachi Healthcare, responsible for placing many of the larger-ticket investments.

“Turkey features prominently in our discussions about placing investments in this part of the world and this is entirely befitting for an emerging market turbo-economy.
that enjoys a clear and robust long-term growth trajectory especially given the sluggishness of many more mature western markets,” explains Refik Öner, managing director Turkey and MISSA at Johnson & Johnson Medical Devices.

“In the other regions and countries that I serve, we deploy an indirect go-to-market model, which entails accessing those markets through distributors. In Turkey, by contrast, we’ve been willing to put down deeper roots. While we’ve not yet gone as far as to opt for any kind of manufacturing site in the country, we have been placing a whole host of other investments from cadaver and animal wet labs for surgical training to Centres of Excellence,” he confides.

Abbott Diagnostic’s managing director for Turkey, Iran, Azerbaijan, Georgia and Northern Cyprus, Yelda Ulu Colin paints a similar picture. “Our organization is actually making sizable capital expenditure (CapEx) investments in Turkey. In other countries we sell equipment and sign service agreements, taking less risk, but here we have the confidence to go much deeper. It’s testament to our trust in the country’s future and support for local players that we judge to have promising prospects. We reckon the fundamentals look sound and therefore we’re willing to enhance our level of commitment,” she reveals.

**Linchpin Between East and West**

Beyond the socioeconomics of a burgeoning middle class, frothy GDP and the projected upswell in demand, Turkey’s natural
The geographical location also plays an ever-present part in many life science companies’ ongoing investment decisions. Not only is the country intricately connected with its neighbours (and beyond) via a customs union with the EU and no less than 28 other free trade agreements with other nations, but it also straddles many of the primary trade routes linking east with west.

“Last year, our global management board opted to turn our Istanbul office into a regional management hub, overseeing 75 countries,” recalls Burak Cem, vice president and general manager of the Danish specialty pharma outfit Novo Nordisk. “This was obviously a massive opportunity for our local organization and testament to the openness and outward facing orientation of the country, but logistically it is really a no-brainer: our superior geographical location enables swift and easy access into and out of the Middle East and Africa with direct flights into almost all the Eurasian markets,” he explains.

The Italian drug maker, Menarini, meanwhile came to very similar conclusions – also choosing to restructure their Turkish affiliate as a regional office overseeing their Middle East and Africa operations. “It’s not just the strategically relevant physical location occupying the crossroads between three continents, but the fact that Turkey society embodies the intermingling between these disparate cultures and customs, and at the same time represents an open, welcoming, generally reliable place to be running a business out of, in what can be, at times a rather unstable and trouble region,” points out Uğur Bingöl, general manager for Turkey, Middle East and Africa.

For Dogan Taskent, board member at the Swiss Chamber of Commerce and head of R&D at Atabay, these sorts of moves are emblematic of a broader trend. “In this day and age, where companies are scrambling to tighten up supply chains in the aftermath of the disruption caused by the pandemic, there is an increased tendency towards nearshoring and considerations such as proximity to valuable market clusters take on additional importance,” he perceives. “For many companies Turkey fits the bill in these respects.”

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State Activism: Vision 2023

One aspect that has really given the Turkish life science sector a shot in the arm has been the vigorous and persistent activism on the part of the government and state apparatus. Dating back to 2016 when the Erdogan administration first launched a domestically popular, but internationally controversial manufacturing localization initiative, Turkish policy makers have recognised pharmaceuticals and medtech as fundamental to the future wellbeing and prosperity of the country.

“The government’s 11th Development Plan, which treats 2019-2023 as a period of profound economic transformation, explicitly highlights the pharmaceutical
industry as a strategic pillar of the national economy that will provide an opportunity for the technological leap that Turkey needs in its development lifecycle,” explains Okan Güner, general manager of Viatris.

Recent years have thus been characterised by a mix of ambitious goal setting and energetic attempts by the state to mobilise the life science community – from private enterprise and international investors to health practitioners and academia – and cajole them into systematically advancing the local sector. The overarching philosophy of Vision 2023 is essentially to “reverse the country’s medicines deficit and render it a net exporter of pharmaceuticals: effectively transforming Turkey into a Eurasian drug development platform and production hub for medium- and high-level technology products,” outlines Burak Dağlıoğlu from the Investment Office of the Turkish Presidency.

“In practical steps this means we have to activate the existing capacity that is not used, and to pivot towards export-oriented growth, while enacting steps that will generate the sorts of advanced technology and know-how that the country needs,” elaborates Tolga Karakan, president of the Turkish Medicines and Medical Devices Agency (TITCK). “And to fulfil these aspirations it will be imperative to bring all stakeholders together and adopt a multidisciplinary approach that transcends private enterprise, the public sector and academia,” he adds.

According to Ümit Dereli, secretary general of the Association of Research-Based Pharmaceutical Companies (AIFD), the 11th Development Plan actually heralds a subtle course correction and change of direction compared to the first half of the past decade. “In short, we’ve now raised our ambitions and are striving to make our country’s industry globally competitive as opposed to just focusing on import-substitution and building a manufacturing hub to supply domestic demand,” he enthuses.

This has gone hand in hand with a massive push to improve the country’s regulatory capabilities and align with international protocols and standards. “The government understands correctly that if we are to achieve global competitiveness, TITCK must become a globally respected regulatory authority that other jurisdictions take seriously,” affirms Dereli.

“I’m extremely pleased to be able to say that our regulator is now very much moving in that direction, and has been looking at Swissmedic, Build Back Better

In most Near East markets, Ministries of Health typically purchase large quantities of hospital equipment using tenders, seeking to acquire the best technology at the best price. In Turkey, however, the authorities have instead resorted to a Public-Private-Partnership (PPP) model in which private investors come in and operate the hospitals.

“So far, we’ve played a major role in quite a number of these PPPs: sharing equity in some construction projects and providing managed equipment services,” explains Nael Dabbagh, general manager for MENEAT at GE Healthcare. On example of note has been the Bilkent City Hospital in Ankara – one of the largest hospitals in the world, with over 3,800 beds and an investment of US $1.1 billion – where GE Healthcare successfully assumed the role of primary supplier for radiology, oncology, and medical devices. “Under the PPP formula, the entire clinical piece remains with the Ministry of Health, but the rest of the operations are outsourced. The results of these partnerships have thus far been deeply impressive: providing a high-quality, modern healthcare system efficiently and at pace,” he notes.

At the same time, Turkey’s health infrastructure drive has also helped to galvanize the country’s construction industry and project influence abroad. “Many of Turkey’s big engineering, procurement, and construction (EPC) companies have learned how to build massive hospitals in a very short span of time – in some cases 36 months – including the financing, design, and execution. Armed with this knowledge and experience, they are now taking their business into Central Asia and African markets as well,” observes Dabbagh.

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Arven Pharmaceuticals is the R&D-based company behind the first biosimilar drug developed and manufactured from cell to final product and the first patented and produced dry powder inhaler in Turkey.
the FDA, and the EMA as exemplars to emulate. TITCK’s recent achievements in becoming a member of Pharmaceutical Inspection Cooperation Scheme (PIC/S) and being admitted to the International Council for Harmonization (ICH) are big news and should not be underestimated. These two steps rank as some of the most important developments for our local industry in recent times and must be applauded,” he insists.

“This is a real gamechanger in terms of our international reputation. Our acceptance as a member of the ICH in May 2020, an organization that aims to harmonize worldwide regulations to ensure that medicines are effective, safe and of high quality, indicates TITCK’s and sector’s commitment to the highest global standards for quality, efficacy and safety in medicines. What’s more, taking a seat at the table has handed us a genuine say over the future direction of the global pharma industry and has empowered us as one of the countries that will determine future rules in this regard,” proudly affirms Tolga Karakan.

The Legacy of Localization

Where materially has all of this left Turkish pharma? In many people’s eyes the localization strategy has been an unmitigated success. Out of the 81 drug manufacturing facilities in the country today, 17 are now owned by multinational firms, according to the Pharmaceutical Manufacturers Association of Turkey (IEIS). Not only have full-scale manufacturing clusters taken shape in places such as the greater Istanbul region and Tekirdag, but the country is now, in volume terms, able to produce almost 80 percent of drugs available on the local market.

Stories abound of recent big-ticket investments from abroad dedicated towards building up a strong in-country manufacturing base. “We’ve been busy putting in place a strong physical footprint with more than 500 employees and a state-of-the-art oral solid dose (OSD) manufacturing site that produces high-quality medicines for cardiology, urology, pain and CNS, catering to both local and global markets,” explains Viatris’ Okan Güner. Meanwhile Redordati’s general manager, Ismail Yormaz recounts how the Italian rare-disease mid-cap has managed to become “one of the shining stars of localization” now producing over 90 percent of the local demand for their specialist products from within the country.

To accomplish this in such a brief time period, the Turkish government had applied both a carrot and a stick approach. On the one hand, the state guarantees seven years of medicine procurement for multinational pharma firms when they partner with a local manufacturer to produce medicines within the country’s borders and has enacted generous tax incentives and land subsidies within so-called ‘free zones’ and ‘organised industrial zones.’ On the other, there have been moves to delist certain foreign derived medicines from reimbursement.

Crucially, however, the reforms have achieved significant buy-in from the private sector itself with many pharma executives judging Turkey to have the right characteristics to be a top-class manufacturing platform. “Turkey’s localization efforts have produced a great many positive outcomes. Moreover, it has become apparent that this is indeed an excellent place to perform manufacturing with an easy access to raw materials, low costs of labour juxtaposed with international standards of quality, a reliable base infrastructure, and a young, dynamic, and highly educated talent pool to draw upon,” Savas Malkoc, IEIS
Too Big to Ignore!

SeokHoon Kang
general manager, Celltrion

Indeed, many companies are also going well beyond just paying lip service to localization. Nestlé Health Science, for example, started out by arranging for a contract manufacturing organization (CMO) to produce enteral nutrition products domestically, but subsequently has been extending that footprint much deeper. “I am proud to reveal that we were the first company to register domestic SKUs for adult medical nutrition with the production of our Resource 2.0 Fibre, and our latest action has been a TL 250 million investment to establish our own manufacturing plant which was opened its doors earlier this year,” enthuses the company’s general manager, Hanzade Yaz.

In spite of the EU’s complaint to the World Trade Organization, we are of the firm opinion that the practice does not contradict international conventions. From our perspective, the government should continue to press ahead with the program so as to increase capacity, raise the bar and attract more foreign investment and technology. Ultimately it becomes a virtuous circle for all concerned,” he argues.

The Korean biopharma play Celltrion serves as a case in point. “Having our own manufacturing facilities within Turkey has most definitely helped with getting through the regulatory process to supply the local market, and we’re now leveraging our fill-and-finish plant to supply the demand coming from our international markets,” notes SeokHoon Kang, the company’s general manager.

Medical Tourism: Putting out the Welcome Mat

Bülent Akarcali
former minister of health; chairman, NBA Consulting

Another key point of differentiation is the new Istanbul airport that serves as a hub for Turkish Airlines, which flies to more destinations non-stop from a single airport than any other airline in the world. “That connectivity makes us very friendly to foreign investment and travel. Two years ago, we received almost USD 2 billion from medical tourism, and there’s absolutely no reason why that can’t triple or quadruple in the future,” he continues.

Meanwhile, Aslı Özelli, executive director of AmCham has noticed that many US companies are now looking to get in on the action by becoming strategic partners for the provision of high-tech medical equipment to furnish the new hospitals and clinics. “The real question is which specific treatments and markets should Turkey focus on so as to not only be a question of price but also of quality,” she wonders.

“Patients from neighboring countries are already coming, but to reach the next level the country should be targeting medical tourists from Europe and the US requiring complex procedures and sophisticated treatments,” she reasons.
“Often in these types of situations one investment leads to another,” opines Philipp Haas, chairman of the board and CEO of DEVA, one of Turkey’s longest-established pharmaceutical manufacturers. “Many companies think about building a production facility without really considering what comes next. They then discover what a great environment this is for an export platform and start thinking about linking it to their global and regional supply chains. Products need to be stored and distributed with good logistic practices, which is why we built our own bespoke logistics hub. We wanted to control the quality of our products for as long as we can and it was the obvious next step,” he reasons.

Export Oriented

Another key feature of the contemporary Turkish life sciences sector has been the increasing tendency of homegrown pharma and medtech companies to start spreading their wings and selling overseas. This is reflected in the trajectory of the country’s trade statistics: pharma exports – the lion’s share of which tend to end up in MENA and CIS – have more than doubled over the past decade with an impressive 60 percent rise registered for the past two years.

Partly this is testament to the maturity of the manufacturing base and the state’s efforts to encourage the practice with a view to narrowing the trade deficit in medicines, but equally it is born out of necessity as a result of the country’s longstanding currency volatility and fixed exchange rate. “The issue is that the Ministry of Health has implemented a special Euro exchange rate which is not related to the reality on the ground because right now the actual rate is 10.3 Turkish Liras per euro, but the official exchange rate is 60 percent of the previous year’s average exchange rate,” observes Recordati’s İsmail Yormaz. “This becomes very challenging at a time where the currency fluctuates constantly. The Lira’s depreciation means that the initial 60 percent can fall to 40-45 percent in real terms which clearly makes it hard for anyone trying to grow their business,” he warns.

Güldem Berkman, general manager of Amgen and its Turkish subsidiary, Gensenta, very much agrees. “All producers, including local manufacturers, depend on the euro and US dollar because 85 percent of the manufacturing cost is related to imported APIs so the exchange rate adjustment can impact profit margins in a big way,” she attests. “Not to mention the fact that payment schemes for medications are usually long-term and not adjusted to inflation.”

In this way, numerous local pharma outfits have been pressing ahead with internationalization strategies. “The domestic price pressures have been driving companies to look abroad because there’s a vast gap between the prices you can secure overseas for medicines compared the ones you obtain domestically as a result of the special exchange rate,” notes Ersin Erfa, CEO of Centurion Pharma. “What’s more there’s a competitive advantage to be had since Turkish products are considered high-quality but are markedly less expensive than European products. In our case we’ve been targeting the Middle East and the Balkans for parts of our portfolio and are continuing to explore new markets.”

Ufuk Kumrulu, the chairman of Polifarma, a leading producer of basic IV and parenteral solutions, concurs. “We believe that the Turkish market is not enough on its own to fulfil our own lofty growth ambitions, so have recently opened an affiliate in Bulgaria to start catering towards the CEE as well. Around 32 percent of our overall sales derived from the export markets last year, but that number increased to over 50 percent in the second quarter of 2021.”

“I don’t think anyone is thinking of turning their backs on the home market where there’s still very good business to be had, but it makes sense to supplement those revenue streams
by taking advantage of the new opportunities that are opening up and to de-risk dependency on a single source,” reasons Süha Taşpolatçoğlu the CEO of Abdi Ibrahim, one of Turkey’s big homegrown success stories.

He sheds light on some of the choices facing Turkish drug makers aspiring to go international. “There are basically two different options: to invest in markets where market entry is relatively easy, that present high profits but equally high risks, or go to markets where market entry is difficult, but which will ultimately allow you to have a predictable business,” he says. “In order to first learn how to do business abroad, we opted to go to North Africa, the Balkans, Azerbaijan and Georgia. We could enter those markets alone as Abdi Ibrahim or by doing joint ventures with local companies and, in the end, we decided to do it both ways depending on the specificities of the individual markets. Now we are finally at a stage where we have the confidence to take on more difficult markets like the US and Europe.”

One Turkish entity that has already reached that stage of maturity is GEN. “We’ve actually been leveraging Turkey’s historical ties and advantageous geographical location to export to CIS countries for many years now, but, since our objective is to be a genuinely world class player, we’re now aiming higher. We’ve already opened an office in Germany and submitted our first generic product registrations to EU countries (namely Germany, Austria, Sweden, Denmark, and Norway) via decentralized procedure. Submissions to the US FDA took place at the end of last year so are expecting the GMP inspections to be imminent,” affirms CEO Abidin Gülmuş.

He reckons that there are bountiful opportunities for those that dare and that his company will find itself exporting a whopping 70 percent of its production within the next three years. “Because we offer difficult-to-make products and are not just pressing tablets we are not aiming to compete in very crowded spaces. Our export strategy is very much based upon high-cost, low-volume drugs,” he discloses.

Therein lies the ultimate obstacle to closing Turkey’s pharma trade deficit. Simply not enough local outfits are yet managing to follow in the footsteps of GEN and manufacture sophisticated, high value products. Despite the great headway made in increasing the volume of Turkish medicine exports, the inconvenient truth remains that almost half of originator drugs as well as vaccines, blood products, and biosimilars still need to be imported. In 2019, imported drugs may have held a market share of only 12 percent in units, but almost 50 percent in value!

“This is precisely why we are pushing so hard with a target-oriented FDI strategy that will provide the nation with a clear road map for attracting value-added, knowledge-intensive investments. Both the share and the sophistication of the exports matter. That’s why the 11th Development Plan explicitly and relentlessly supports R&D production activities from SMEs, encourages the creation of biologics and provides purchase guarantee for advanced technology investments,” argues Burak Dağlıoğlu of the Investment Office.

Pivoting Towards Biotech

Turkey’s budding biotech scene certainly has come on in leaps and bounds in recent years. According to the Turkish Biopharmaceuticals platform, some 22 pharma companies are currently working on 2 reference biotech drugs and 40 biosimilars ready to launch by 2024. What’s more the country now boasts 35 accredited pharma R&D labs and 14 dedicated university research centers, as well as accelerator incubation platforms such as Hacettepe Teknokent, EGE Teknopark, BIGGHEALTH, Lifesci, and Inovita.

At the same time, the scope for improvement remains immense. “To put everything in
proper context, Big Pharma habitually spends around 15 percent of their revenues on R&D, but in Turkey that number languishes at only around 5 percent despite the fact that there are sufficient skilled scientists and researchers coming out of our universities,” laments the IEIS’s Savas Malkoc.

“For Turkey to forge a globally competitive pharmaceutical industry, it’s absolutely imperative to provide an environment where start-ups can be identified and supported,” acknowledges the AIFD’s Ümit Dereli. “The days when large corporates used to spearhead cutting edge innovation have come to an end. Nowadays, that task very much falls to small and mid-size biotechs, so if Turkey wants to properly get on the innovative biologics bandwagon, it has to cultivate the right sort of enabling ecosystem and a cadre of true entrepreneurs,” he adds.

“Frankly, at the moment, Turkey is generally not considered particularly competitive in biologics,” concedes Süha Taşpolatoğlu of Abdi Ibrahim. He believes that the best way to turnaround this situation would be for more Turkish entities to establish joint ventures with foreign biotechs so that they could better learn the ropes.

“In our own case, we took the strategic decision to collaborate with other companies to acquire the relevant know-how and opted to partner with an American bio start-up called Ocugen which is developing biotech eyecare products. In the same vein, we purchased a 28.5 percent stake in OM Pharma, a Swiss biotech," he recalls. “When you look at the last two decades of the Turkish pharmaceutical industry, you will observe that many Big Pharma outfits, particularly from Europe, acquired local players to enter and compete in the Turkish market. For example, Swiss investors bought DEVA, Italians acquired Ibrahim Etem and the Czechs bought Eczacıbaşı. The OM Pharma acquisition is the first time a Turkish company has reversed the trend and bought a European entity,” he points out.

The story of İLKO Pharmaceuticals, currently one of the only homegrown Turkish drug maker that can develop bio-betters all the way from the master cell line until finished product somewhat supports that hypothesis. “We were quick out of the blocks to establish a joint venture with Genexine, a South Korean biotech and together with

NCDs: Last Chance Saloon

Turkey recently gained notoriety as registering the highest prevalence of diabetes in the whole of Europe (14 percent of the entire population), with many estimates saying that one-third of Turks are now overweight or clinically obese.

“Since obesity requires a multidisciplinary approach, we are working with the Minister of Education to raise awareness about healthy eating and the consequences of poor lifestyle choices. However, local studies of the pandemic are suggesting that people have gained six kilograms of weight on average so you can imagine the formidable task we have ahead,” exclaims Burak Cem of Novo Nordisk, a specialist in countering diabetes.

“Fortunately, Turkey is one of five countries that have accepted obesity as a chronic disease and the government is opening obesity centres that help patients with diet, provide psychological aid and treatment. We are the only company investing heavily in that area which is why we keen to collaborate with the authorities in launching a new program specifically aimed at tackling childhood obesity,” he claims.

Luckily extra support is arriving to help the Turkey get a grip on the broader proliferation of non-communicative diseases (NCDs) which in total account for 89 percent of all deaths in the country. Viatris, a new entity that was formed globally in November 2020 as a result of the merger between Pfizer’s Upjohn portfolio and Mylan will be mobilizing its full range of solutions along the pharma and healthcare continuum to help bring about a change in behaviours and treatment paradigms.

“With our global portfolio which comprises more than 1,400 molecules across a wide range of therapeutic areas from cardiovascular health to oncology, we will not just be offering the medications themselves but a whole host of beyond the pill solutions and services encompassing diagnostics, health literacy support and digital tools to help patients better manage their health,” assures Okan Güner, the company’s managing director.

SÜHA TAŞPOLATOĞLU
CEO, Abdi Ibrahim
them, we are developing bio-bett- ters. For the past five years, we’ve been accruing the requisite know- how that will allow us to compete and master this segment,” proudly recounts the company’s CEO, Hatice Öncel.

**Biosimilars: The New Gold Rush?**

In fact, many Turkish companies that seek to build their own innovative biologics capabilities are first looking to developing biosimilars as a way of getting up to speed with the new technology. “Quite a few local outfits are betting on biosimilars as a production opportunity. So far, around 19 companies have invested in biosimilar production within Turkey, but the penetration continues to be underwhelming and a market remains dominated by big multinationals. At Gensenta, by contrast, we are lucky to be able to draw upon Amgen’s quality, portfolio and engineering capabilities,” details Güldem Berkman.

One company that really has managed to raise eye-brows is Istanbul-based Arven Pharmaceuticals, a subsidiary of the renowned Toksöz Group. In 2016, the company obtained marketing authorization for the biosimilar of Filgrastim, the first such product to be developed and manufactured from cell to final product entirely within Turkey. “What really sets us apart is that our team is capable of developing from upstream all the way to industrialization. Most Turkish companies with investments in biosimilars have failed to look at the strategic value of the overall process and have just concentrated on the fill and finish component,” observes Zafer Toksöz, the company’s president and founder.

“By going the extra mile, we are engineering all sorts of fresh capabilities. For instance, the technological infrastructure required for biosimilars happens to also be used for recombinant DNA vaccines. This is how we were able all of a sudden to invest deeply in new injectable lines for high-scale products earlier this year,” he explains.

The company also stands out for successfully adapting its business model to better align with the local market dynamics. “Two years ago, we invested in trastuzumab and bevacizumab – two monoclonal antibodies – which were ready to undergo clinical trials. Unfortunately, the reimbursement system in Turkey made prices for those products too low for us to consider it a feasible investment. The government is buying most of these products through tenders at a low pricing strategy. The issue is that foreign entities that own the originator product see Turkey as 1 percent of the global market so are often willing to sell it at a cost, with extremely low margins or at the breakeven point, but Turkey represents 100 percent of Arven’s market so that avenue was, in practical terms, closed to us,” regrets Tokzos.

“One alternative could have been to sell them abroad but globalizing a single biosimilar product like that often requires a USD 30-40 million investment just to get it through the clinical studies. Instead, we decided to halt our own development of biosimilars and become a high-level and sophisticated CDMO, offering our capabilities to develop and manufacture for other companies. Nowadays, we can offer a unique set of biosimilars capabilities to any organization that wants to enter the business but does not have its own manufacturing or development know-how in Turkey,” he concludes.

“Right now, is an incredibly fascinating and formative period for Turkish pharma as our flagship and iconic companies venture into new areas,” reflects Dogan Taskent. “The important thing is they are giving it a go. As I perceive it, the critical issue is the scale-up know-how. We are still right at the beginning of the learning curve. While I happen to serve as R&D chief for Atabay, I don’t see Arven as a competitor, but as a potential collaborator and a company that’s doing a great job for the reputation of Turkish biologics. Now is the moment to all pull together, share the knowledge and to build a rising tide that lifts all boats,” he appeals.
Clinical Trials: Untapped Potential

However, if Turkey is truly serious becoming internationally competitive in life science innovation, it will need to perform better when it comes to clinical trials. “In order to create new molecules and innovate you have to invest heavily in clinical trials from Phase I to Phase IV because manufacturing constitutes only the very last stage of the cycle...it’s important to maintain strength and depth right along the pharma value chain so that all elements hang together properly,” counsels Novo Nordisk’s Burak Cem.

Following that logic, the Danish speciality drug maker helped drafted a plan for a partnership with the Health Institutes of Turkey (TUSEB) to exchange researchers with Denmark and bring additional know-how to the country. “Globally, over USD 160 billion is invested a year by the industry in R&D, of which Turkey accounts for only around USD 130 million, so it’s important that we help turn this situation around. Focusing on the clinical trials space is a great place to start,” he insists.

Novartis managing director, Avinash Potnis very much agrees. “Clinical trials can bring a real boost to the entire local life science ecosystem by exposing clinicians to cutting edge technology and by presenting opportunities for local doctors to become better engaged with the global healthcare landscape. It can be a real catalyst and accelerator to further advancement” he notes.

“Clinical trials make up more than 60 percent of all R&D investment, therefore putting a focus on them certainly makes a great deal of sense,” reinforces Janssen’s managing director.
“Turkey’s existing regulations are simply not flexible for the types of studies that are increasingly in vogue such as adaptive clinical trials. These sorts of designs are now deployed frequently around the world for studies in haematology, oncology and vaccines, so there’s an urgent need for Turkey’s educational and ethical committees to organise themselves better if we are to remain competitive,” he warns.

One big step forward has been the country’s accession to the ICH. “The consistency and functionality of legal regulations and international standards create a strong environment of trust in clinical trials coming out of Turkey. ICH membership serves to reinforce international confidence in Turkey’s processes and therefore should make us considerably much more attractive,” insists Tolga Karakan of the TITCK.

And indeed, quite few multinationals have consequently been ramping up their in-country clinical trials activity. “The prominence of Turkish key opinion leaders within international advisory boards and the recent regulatory alignment have definitely served to boost the research ecosystem... currently we are running some 55 clinical trials in 267 investigator sites that are helping over 2,000 patients,” declares Bayer’s Ingrid Drechsel.

MSD meanwhile has some 90 active studies in play with at 63 unique sites, while Novo Nordisk continues to invest big having spent over TRY 121 million on Phase I to Phase III trials over the past 5 years. “I’m proud to reveal that almost 10 percent of our organization works in the clinical research department and that the Turkish organization has become the clinical development centre for the entire region, coordinating Algeria, Morocco, Lebanon and Ukraine. We have 250 active researchers in Turkey running 12 international clinical studies across 88 centres,” says Cem.
The Path to Greatness

What, then, is the overall assessment of the state of the Turkish life science industry on the eve of the Republic’s grand centenary? For a start, the numbers don’t lie: Turkey is too big and too strategically relevant to ignore. “At the end of the day, all of our big brands and products are available in Turkey. Of course, every country experiences its own difficulties, and the exchange rate and pricing issues sometimes make life tricky, but the opportunities out here are nonetheless unmissable. This is a market where Bayer will always play a role, regardless,” exclaims Ingrid Drechsel.

“The key to doing well out here is being able to manage short cycles while keeping your eye on the long-term ball,” advises GE Healthcare’s Nael Dabbagh. “After many years working in the Turkish market, I can confirm that it is possible to have a highly successful business here. The Turkish people are extremely resilient, which you can see from the overall positive trend of development and growth over the past decades.”

“Turkey is often thought more in terms of the challenges it presents than the opportunities it serves up, but the global industry would be misguided to imagine Turkey as a problem child,” declares Novartis’ Avinash Potnis. “The vast population, robust healthcare infrastructure and universal coverage make it one of the most advanced pharma markets in its region. When our CEO Vas Narasimhan visited in 2019 he was wowed by what he considered to be a rare and unique value proposition: bringing European perfection at an affordable cost. This country is going places and Novartis will be there to assist it every step of the way!”

### TOP 10 PHARMA COMPANIES IN THE TURKISH MARKET (MAT SEP 2020-2021)

<table>
<thead>
<tr>
<th>COMPANY</th>
<th>SALES, USD M</th>
<th>SALES GROWTH</th>
<th>UNIT GROWTH</th>
<th>MARKET SHARE MAT1</th>
<th>MARKET SHARE MAT2</th>
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<tr>
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<tr>
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<tr>
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Source: IMS
Healthcare: Investment, Not Burden

Demet Russ discusses her return to the country after 25 years abroad, having worked for Johnson & Johnson in different local, regional and global roles in Germany, Belgium, France and the US. She explains Janssen’s broad presence in Turkey, their focus on clinical trials and the “fantastic” data infrastructure available in the country.

Can you briefly introduce your background, long career with Johnson & Johnson and how the decision to come back to your home country came about?

DEMET RUSS (DM): I am Turkish by origin and received my bachelor’s degree from Boğaziçi University. My first career step was at McKinsey & Co. where I worked on projects across several industries and sectors, including financial services, high-tech, transportation, infrastructure, retail, and healthcare. During that time, I discovered that my passion was healthcare and the pharmaceutical sector.

I joined the finance team at Johnson & Johnson in 2005 in Germany and for the next 15 years, I worked in seven different roles across four countries, including at a regional and global level.

In January 2020, I was appointed to my current role as Managing Director for Janssen Turkey... I came back to Turkey after 25 years and, having benefited from the public education system, I have always felt indebted to Turkey, so I am happy to be here to bring innovation to access of Turkish patients.

Coming back to Turkey after 25 years, what type of organization did you encounter?

DM: Janssen has been active in Turkey for 22 years and sees the country as a major strategic healthcare market, as evidenced by the fact that it has brought 40 innovative therapies to the country’s healthcare market.

Janssen Turkey has a strong clinical trials footprint; the number of clinical trials grew by 50 percent in the last three years, and we invested a total of USD 50 million in the last decade. We are among the top 5 companies by R&D expenditure in Turkey with 47 ongoing trials in over 200 centers. On top of that, we produce about 70 percent of our local volume in the country and are currently working to localize two new products.

How strong is Turkey’s healthcare system as it relates to its capacity to introduce innovative therapies and what are some of the areas that the overall system can improve on?

DM: Turkey has a strong healthcare infrastructure and universal health insurance coverage that provides accessible, high-quality healthcare services for all. The healthcare system proved its resilience during the pandemic.

I believe it is important to look at healthcare as an investment, rather than a burden on the public budget: an investment in the population, their health and quality of lives. A recent analysis shows that every dollar invested in healthcare creates a return of two and a half dollars for the economy. The COVID-19 pandemic exemplifies this because, according to an analysis from The Economist, a vaccinated person could have saved the economy USD 2,900. Those are all global studies but certainly apply to Turkey.

Moreover, Turkey has a fantastic data infrastructure; I have worked and been a patient in several countries and never seen such a connected system. It is an efficient system that has been on display during the vaccination program. The existing data infrastructure can be used to create real-world evidence benefiting the development of the innovation ecosystem. 🌟
As a top 5 pharma company in Turkey, how wide is Bayer’s presence in the country and what role does it play for the global organization?

INGRID DRECHSEL (ID): Bayer has been in Turkey for over six decades, benefiting from the good relationship between Germany and Turkey. This relationship should continue and be strengthened because both countries are learning from each other. We were in fifth place as of 2017 but moved to number three a few months ago. Of course, the pandemic had an impact, but we are getting back on track thanks to our innovative products.

Bayer is a very innovative company that has invested in Turkish talent and ideas; we have a crop science production and development site as well as a strong local manufacturing footprint for pharma products here, producing 40 percent of the products sold in the local market. Besides our headquarters in Istanbul, we currently have eight regional offices in order to serve the whole country adequately.

Today, Turkey is very involved with Bayer’s innovative products from the beginning. I believe that the prominence of Turkish key opinion leaders within international advisory boards has boosted the research ecosystem, not to mention the cultural similarities and geographical position; we have more than 55 clinical trials in 267 investigator sites, helping over 2,000 patients.

Another important topic for us is e-health and telemedicine, something that the government also has on its agenda. Bayer implemented a couple of pilot programs last year on this topic, specifically on women’s health and oncology, two different fields where we can link patients with healthcare professionals. Improving and developing e-health cannot be done overnight because there are plenty of hurdles, but it is important that the industry plays a fair role in developing it.

Last year you presented a localization project to produce a cardiovascular enterprise in the country. What can you tell us about that project?

ID: The localization project followed the Turkish government’s strategy to introduce more local production to the country. Since Bayer does not have its own production facility for pharmaceuticals in the country, we are producing and investing through partners.

The initial idea is to supply local demand, but you never know what the future holds. The product in question has a strong market position in many countries that have approached us, asking if it is possible to manufacture it for them as well.

How is your objective of introducing Bayer’s complete portfolio to the country affected by the pricing system?

ID: All our big brands and products are available in Turkey. Of course, every country has its own difficulties, it is normal, so we have to overcome the challenge and turn it into opportunity. There are always ups and downs, but Turkey has a large and educated population and a high-quality healthcare system. Bayer will always play a role, regardless of the pricing system, but it is true that we should find common ground with the government because companies need to have a successful business in order to help patients. Science for a Better Life is our mission.

Ingrid Drechsel, Bayer

Leveraging the Turkey-Germany connection

Ingrid Drechsel discusses the advantages of Bayer’s longstanding presence in Turkey with a track record of six decades. She explains their continuous investment in localization, clinical trials and e-health.
Becoming the clinical trials country leader in the region has been set as a primary goal for Turkey’s pharma industry to achieve global competitiveness. The government’s strategy is to increase its share of global clinical studies both in numbers and investment. Today, the country occupies the 26th position with 529 clinical trials in 2020.

On principle, that strategic decision makes sense since R&D is considered one of the most valuable investments pharmaceutical companies can provide as it relates to exposure to innovation for healthcare practitioners, researchers and patients. Within that paradigm, clinical trials are a natural proposition since over 60 percent of total pharmaceutical R&D investment is spent on them (phases I-IV).

The discrepancy between Turkey’s 26th global position in clinical trials and the size of the market, 18th globally, is something the industry is aiming to address. “At AIFD, we believe that the country can increase the clinical trials volume by three times to enter the global top 10,” says Janssen’s Demet Russ, who is also a board member of AIFD, the association representing multinational innovators.

As of June 2019, the total economic annual value of clinical research in Turkey is estimated at USD 327.7 million, according to IQVIA.

Government authorities, for their part, are embracing that proposition. According to the president of TITCK, Turkey’s regulatory body overseeing clinical research, the country has implemented initiatives in recent years to improve the clinical trials ecosystem, including a “solid legislative infrastructure” that follows European Union and ICH standards.

“[Turkey] has become a strong candidate for multinational clinical trials... Consistency and functionality of legal regulations and international standards create an environment of trust,” contends Dr. Tolga Karakan.

Not so fast...

“Changing regulations or laws in Turkey is difficult and takes time,” argues Dr. Hamdi Akan, president of Turkey’s Clinical Research Association, explaining that regulations are not “flexible” enough for adaptive clinical trials, for example, which are designs used increasingly for hematology, oncology or vaccines.

The vast majority of clinical trials conducted in Turkey are phase II and III studies, accounting for 93 percent of the total industry-sponsored trials, with Phase I being only 1 out 100. The reason, Dr. Akan says, is that accreditation of the centers from TITCK is not required for phase II-IV as they are with phase I trials.

He does, however, applaud Turkey’s adherence to the International Conference on Harmonization (ICH), saying that the ecosystem learned “a lot” through the process of harmonizing laws and clinical trials guidelines with EU regulations.

We believe that the country can increase the clinical trials volume by three times to enter the global top 10”

Demet Russ
JANSSEN
Dr. Akan believes that while medical infrastructure in Turkey is already globally competitive, the system needs more dedicated places to conduct clinical trials, an institutional centralized site coordinator, training programs, as well as transparent disclosure of clinical trials in a database, something that TITCK successfully developed but could be further improved.

The real prize?

While USD 327 million in R&D per year is quite an investment, a few stakeholders argue that more should be asked from multinational pharma companies than clinical trials. Of the 34 R&D centers in Turkey owned by private companies, less than 3 are owned by multinationals, Sanofi and Amgen amongst them.

“R&D centres are the real prize, where talent is developed, innovation created, and know-how distributed. People that leave those centres can later go to Turkish companies to advance their careers or become entrepreneurs, sharing the knowledge with the local ecosystem,” says Dogan Taskent, R&D head of Atabay.

Skeptical of Big Pharma’s proposition, Taskent argues that multinationals in Turkey promote their contribution in clinical trials, but “fail to mention that [they must conduct them] in order to sell the products in Turkey... Yes, clinical trials bring money to the country, but they are also a double-edged sword because they experiment with human beings that may or may not benefit.”

Nevertheless, he admits that clinical trials “are a necessary step to ensure that patients receive safe and effective drugs, but ethical grey areas exist,” and encourages multinationals to conduct more comprehensive R&D projects to leverage the low budget required for them in Turkey while maintaining the same quality.

Making a counterargument, industry executives suggest that convincing headquarters to open their wallets is a tough sell in a country where pricing pressure is constraining their growth.

Avinash Potnis from Novartis indicates that the pricing challenge could discourage companies from launching new therapies, thus affecting clinical trial investment “because it would not be ethical for companies to bring innovative treatments only to have those patients not be able to continue the treatment post-closure of trials.”

Tangible results

“Turkey is an important clinical studies hub for the organization due to the great capabilities of the centers and efficacy results,” says Güldem Berkman from Amgen, which owns Gensenta and its R&D center, and is investing in phase I and II trials.

Takeda is running 15 clinical trials in oncology, hematology, genetic diseases, and immunology; Bayer is doing 55 in 267 investigator sites; Novo Nordisk has 250 active researchers running 12 studies; and MSD is conducting 93 studies.

Janssen has invested USD 50 million in the last decade and has 47 ongoing trials, a number that has grown 50 percent in the last three years.

| TURKEY’S GLOBAL RANKING IN THE NUMBER OF ACTIVE CLINICAL TRIALS |
|-----------------|---|---|
| Overall ranking  | 26 |
| Relative to population | 56 |
| Relative to GDP | 62 |
| Relative to pharmaceutical market size | 40 |

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REGULATORY REVIEW TIMELINES (NUMBER OF DAYS)


ANNUAL INVESTMENT AND NUMBER OF CLINICAL TRIALS (2012-2020)

Source: AIFD

PHARMACEUTICAL R&D INVESTMENT BY FUNCTION

Source: PhRMA Annual Membership Survey 2018
Fighting Turkey’s Diabetes & Obesity Crisis

Dr Burak Cem outlines Novo Nordisk’s big bet on Turkey as a future regional hub through deep investment in clinical trials, localization and an operational hub overseeing 75 countries. After almost two decades working with the Danish diabetes and obesity giant, he illustrates the crucial role that the company has to play in the country with the highest incidence of diabetes in Europe.

Last year, Novo Nordisk made Istanbul a regional management hub, overseeing 75 countries. What was the unique offering of Turkey that you think helped the company take this decision? 

BURAK CEM (BC): There are a few reasons, one of them is that we are right in the centre of the Middle East and Europe, providing the country with a superior geographical location that allows us to access the Middle East and Africa easily with direct flights to almost all countries in the area. The second one is that there is a strong labour force of well-educated talent that are looking for a job in an international environment; the benefit-cost ratio is very high in Turkey because labour is not as expensive while having the same quality. This new arrangement has created a special opportunity for the Turkish organization, as well.

Speaking about opportunities for the Turkish organization, the country has the highest prevalence of diabetes in Europe with around 14 percent and a recent report stated that it will increase to 25 percent by 2025. How would you characterize your current position in this market environment? 

BC: We have been a market leader for a long time in diabetes and in the insulin busi-
ness. Coincidentally, this year we celebrate 100 years of the discovery of insulin, which was discovered following the ideas of a Canadian orthopedic surgeon named Frederick G. Banting in 1921.

We currently have 53 percent market share in the insulin business and around 22 percent market share in diabetes. We are the only company to provide insulin for every type of patient, from children to the elderly. We have created great partnerships with the government and civil society to increase awareness and continuous medical education for doctors.

As you pointed out, Turkey has the largest diabetes prevalence in Europe with 14 percent and, to make things worse, one-third of the population is living with obesity. Around the world, two billion people are overweight and 650 million are obese but, sadly, Turkey is number one in Europe and number four in the world. Two-thirds of the Turkish population are either living with obesity or they are overweight which presents a great need to tackle this serious problem to change the life of millions of people.

Since obesity requires a multidisciplinary approach, we are working with the Minister of Education to generate awareness in the lives of people with obesity about healthy food and the consequences of poor lifestyle choices. Recent studies of the pandemic have shown that people have gained six kilograms of weight on average so you can imagine the work we have ahead.

Globally, it has been difficult to move the obesity conversation from the aesthetic to the clinical setting. To what extent has this been the case in Turkey?

**BC:** You are correct about the global conversation about the aesthetic element, in fact, obesity is a curable chronic disease. Unfortunately, in Turkey two-thirds of the public are either people with obesity or overweight which means that we are in a crisis and have not had the luxury of having that conversation; for us, there is no question, we have to act. The country has to help people make lifestyle changes with diet and exercise and use pharmaceutical products as a complementary therapy to avoid needing surgery.

Fortunately, Turkey is one of five countries that have accepted obesity as a chronic disease and the government is opening obesity centres that help patients with diet, provide psychological aid and treatment.

**Your colleagues from the industry are speaking about how Vision 2023 is shifting from a focus on manufacturing to include more clinical trials. How do you evaluate Vision 2023 from a company perspective?**

**BC:** Indeed, the government had a focus on localization and gave some incentives to achieve that because they wanted to have the know-how and secure product delivery. It is true that Turkey is a great hub for localization since 80 percent of the medicines used are produced in the country but there are two issues: new molecules and exportation.

Fortunately, everyone understands that in order to create new molecules and innovate you have to invest in clinical trials from Phase I to Phase IV because manufacturing is the last stage of the cycle. Following that logic, we drafted a plan for a partnership with the Health Institutes of Turkey (TUSEB) to exchange researchers with Denmark and bring know-how to the country.

In terms of manufacturing, the government’s interest goes beyond producing for local consumption and would like to be an exporting hub. Internally, we found common ground with them in this regard and submitted our application to get a localization project approved that will bring a big investment and new employment potential over ten years to bring production and use it to export to the region.

Taking into account the big investment in localization, management hub and clinical trials, we decided to take a bigger approach and created a project to make Turkey a strategic hub for Novo Nordisk. If we can make it happen by 2023, it will coincide with the 100 anniversary of both Novo Nordisk and the Republic of Turkey.

The future of the local pharmaceutical healthcare system will highly depend on the adoption of new innovative therapies to the Turkish healthcare system in parallel to developed countries. Hence, in our opinion, the better way to ensure long term sustainability of the public healthcare system and attain the most advantageous patient outcomes in therapy areas where innovative therapies changed the prognosis of the diseases would be to implement value-based pricing in reimbursement decisions of innovative products.
Almost two decades after initiating large-scale health system reforms, Turkey has consolidated the provision of universal healthcare coverage to over 95 percent of the population. The effort, part of the country’s Health Transformation Program introduced in 2003, has been commended by international organizations across the world. But today, as citizens reap the benefits of these reforms, industry stakeholders are raising concerns about some of their implications.

After all, Turkey’s universal healthcare coverage is, in part, being sustained through some of the lowest pharmaceutical prices for countries in similar socioeconomic situations. Today, Turkey spends less than one percent of its GDP on pharmaceuticals, way below the OECD average, and the sustainability of the ecosystem is in question due to low pricing, delayed access and a limited budget, according to the general manager for Novartis Turkey, Avinash Potnis.

The pricing for medicines in Turkey is reference-based, whereby the least expensive ex-factory price in two of five listed EU countries is taken as the price. The basket of reference countries includes Spain, France, Portugal, Italy and Greece but the Ministry of Health (MoH) has discretion to change reference countries, provided it makes an announcement at least two months before.

The second step in the process, and one that is often questioned by executives, is the implementation of a special Euro exchange rate set by the MoH since all prices are converted into Turkish liras. “The Ministry of Health has implemented a special Euro exchange rate which is not related to the real exchange rate because, today, the rate is 10.3 Turkish Liras per Euro, but the official exchange rate is 60 percent of the previous year’s average exchange rate. This becomes very challenging at a time where the currency fluctuates constantly; the Lira’s depreciation means that the initial 60 percent

“[Bayer] will always play a role, regardless of the pricing system, but it is true that we should find common ground with the government”

Ingrid Drechsel
BAYER
Market Challenges

can fall to 40-45 percent in real terms,” explains Recordati’s İsmail Yormaz.

Ingrid Drechsel, Bayer’s pharma head for Turkey and Iran, paints a similar picture, highlighting that the German company will “always play a role, regardless of the pricing system, but it is true that we should find common ground with the government because companies need to have a successful business in order to help patients.”

While most executives concur that pricing is an issue that needs fixing, some are more optimistic and do not believe that it amounts to an existential crisis.

“Turkey is a promising place to do business regardless of the pricing issues and the current backlog in registration. There is a generation of young talent that is very capable. The economy will continue its upward trend, reflecting the resilience of the Turkish people,” says Menarini’s Uğur Bingöl.

Stroking a more sympathetic tone, he alleges that companies cannot leave because there are business principles involved, “we are here to serve patients and save lives… we have to stand with the country in the bad times just as we have done during the good times.”

But even Bingöl concedes that while Menarini is not holding back, “it could be a problem in the future... We are having continuous conversations with the government so that we can go from survival to investment mode.”

The upside: rising exports

A positive side effect appears to be the increase in exports as companies with manufacturing capacity in Turkey look abroad for better prices.

“I believe that the domestic price pressure has been driving companies to sell products abroad; that is why medicine exports have consistently increased over the past five years. There is a huge gap between the prices you get abroad for medicines from the ones you get in Turkey... The trend of companies manufacturing in Turkey for foreign markets will continue in the coming years,” says Savas Malkoc, secretary general for IEIS.

Searching for solutions: value-based healthcare

The solution to the pricing dilemma, according to Avinash Potnis, is not to look at pharma products from a price perspective alone, but instead to take a value-based approach.

“For example, the value of our chronic heart failure therapy is not measured by the price but by the time a patient stays out of the ICU, reduced mortality and finally the quality-of-life patients gain,” he notes, adding that the “artificial exchange rate” should be taken out immediately since it is almost half of the actual rate.

Burak Cem, general manager for Novo Nordisk, a company that has found a key market in Turkey given its high prevalence of diabetes and obesity, also contends that the best way to ensure long term sustainability of the public healthcare system and attain the most advantageous patient outcomes would be to implement value-based pricing in reimbursement decisions of innovative products.

The upside: rising exports

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<thead>
<tr>
<th>PHARMACEUTICAL PRICING</th>
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<tr>
<td>Same MoH price as EU due to patent protection</td>
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<td>Due to conversion rate set as 3.82 TRY</td>
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<td>TR price after SSI discount</td>
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<td>Due to conversion rate set as 3.82 TRY</td>
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<td>MoH price due to beign generic product</td>
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10€
4.2€
2.5€
1.8€
2.5€
6€

-58%
-41%
-28%
-53%
-40%
Looking for a Silver Lining

İsmail Yormaz explains the complex pricing system in Turkey, its implications for multinational companies, and suggests a few steps to improve the situation. In addition, Yormaz highlights the importance of innovation and accessibility as the main learnings from the COVID-19 pandemic.

Recordati’s Turkish organization remains one of the most profitable for the group, how would you characterize its importance?
İSMAIL YORMAZ (İY): We are one of the top 10 countries for the Recordati group in terms of revenue. However, in Turkey, there are some issues that the country needs to correct, the exchange rate and overall economy for example, because they often detract from our many achievements. While the Turkish pharmaceutical market has recorded significant growth in the last 6 years, its place in the range of 6-7 billion dollars does not progress when evaluated in terms of dollars (according to IQVIA data). This is a purely macroeconomic exchange-related subject, but nonetheless a mistake that has impacted the industry.

As a company, we were very flexible during the pandemic, but I cannot say the same for the regulatory environment. I want to be optimistic that things will go back to normal soon but the regulatory process in Turkey was delayed in the last 15 months, a situation that will prevent many good projects and new launches from moving forward. In the last 15 months, we have managed to launch only one of our line extension products. We cannot forget that the world is very competitive, and the pandemic has highlighted the need to be fast and agile; it is a lesson that the Turkish regulatory environment has to learn. It is also something that applies to other areas within healthcare such as the pandemic response and vaccination.

Besides the regulatory bottlenecks, you have also talked about issues around pricing in the past. Can you explain how the Turkish pricing system works?
İY: Pricing is currently the most important subject and challenge for the Turkish pharma market. First, pricing is reference-based, and the Turkish authorities have chosen a basket of countries that include Portugal, Spain, France, Italy and Greece. Greece, for example, takes the average of the lowest two countries which means that Turkey is effectively taking...
the lowest two European prices. Similarly, in France, changes to article 66 have made a significant price reduction which is automatically impacting the prices in Turkey.

Secondly, the Ministry of Health has implemented a special Euro exchange rate which is not related to the real exchange rate because, today, the rate is 10.3 Turkish Liras per Euro, but the official exchange rate is 60 percent of the previous year’s average exchange rate. This becomes very challenging at a time where the currency fluctuates constantly; the Lira’s depreciation means that the initial 60 percent can fall to 40-45 percent in real terms.

Thirdly, the reimbursement system also presents a complication. Around 90 percent of pharmaceuticals are covered by Social Security, but they employ discounts depending on their price level and whether they are original or generic. That means that they put additional discounts on top of the exchange rate. It is true that patients end up receiving some of the lowest prices in the region but the burden for pharmaceutical companies can become too big.

How can that pricing system become sustainable for multinational companies?

İY: That is the big question for the Turkish market, a question that should read “sustainable... until when?” The Turkish authorities continue to be content with the current system because it has been sustained until today. The question the industry is asking itself is for how long this will be sustainable, and, frankly, I do not know. Today, the devaluation speed of the currency and the economic hurdles are making it hard for companies to thrive and compete.

Fortunately, Recordati has a relatively strong financial situation, and we are always looking to profitability. However, we do have a couple of products with a negative margin, and I am still fighting for a better price. Additionally, I am negotiating to decrease the expenses of the products.; It was not an issue five years ago, but a lot has changed since.

Every executive in the Turkish Pharmaceutical Industry might as well have a mathematics degree because all of them know the pricing, gross margin and calculations.

I do not think that the contribution of the pharmaceutical industry to public health is adequately understood in Turkey. We have very successful politicians and bureaucrats in the country, so, if we can work together on this issue and reach a fair pricing system, we will see that the patients benefit the most.

Looking to the future, what are your priorities and strategy in the next five years?

İY: COVID-19 has taught the industry two important lessons: the importance of innovation and accessibility. In less than 12 months, the industry has developed four or five vaccines which is a total success. Accessibility, on the other hand, remains the big challenge because the distribution of the vaccines has been uneven. Innovation is profitable, yes, but we also have to keep in mind the distribution of economic value in the coming years.

This is a great opportunity for the Turkish pharma industry to increase its geographical presence; I am sure that things will change significantly in the Turkish pharma environment in the next few years. Recordati continues to grow in Turkey because we have a strong pipeline. We plan to launch five to six major projects in the next months. For example, this year Recordati made a licensing agreement with Tolmar to commercialize Eligard, an important uro-oncology product, which will now be delivered to the patients by Recordati. We will also introduce a CNS product most likely in the next year, and two rare disease products from the Recordati Rare Disease business. From a turnover point of view, we are in great shape and will continue expanding our presence in the country. 🌟
According to recent disclosures, Boehringer Ingelheim Turkey’s 2020 results were very positive, growing 54 percent and ranking within the top 15. Can you explain what drove this performance?

**EVREN ÖZLÜ (EO):** As General Manager, one of my primary objectives was to organize and deploy our teams efficiently to execute our new product launches, and in doing so, grow our presence, footprint, and reputation within the country. Agility is of paramount importance and the COVID-19 pandemic has engendered huge changes in market dynamics across all industry sectors.

We have successfully navigated the challenges through our corporate mindset of flexibility and have responded to the drivers of change through experimentation... We took prompt action to shift our activities from face-to-face to digital interactions to maintain operations and ensure business continues despite the unprecedented pressures faced. Our omni-channel digital engagements were conducted through websites and applications that what have put to the service of our stakeholders to provide uninterrupted advisory service. This approach has enabled us to navigate the challenges of the COVID-19 pandemic and secure double-digit growth in 2020, but more importantly continue to serve our customers and patients through unprecedented times.

To better understand the launch process you have explained, what is your focus in terms of therapeutic areas in Turkey and how do you expect the market to evolve?

**EO:** The two main therapeutic areas for Boehringer Ingelheim in Turkey are diabetes – which we categorize under ‘metabolism’ – and specialty care, which encompasses rare diseases such as idiopathic pulmonary fibrosis (IPF) and scleroderma – interstitial lung disease. Diabetes in particular will continue to be a focus area for us in Turkey, given its high and growing prevalence.

We will continue to invest further in Turkey, as we strongly believe in the bright future of the market. Based on the country’s registration timelines and activities, the next five years will see us introducing products in line with our organization’s global investment and portfolio.

After joining the Turkish affiliate to execute an intense product launch phase, how challenging has that experience been?

**EO:** Preparation is key when it comes to product launches within the pharmaceutical industry, and such level of preparedness requires time and effort. In addition to preparation, we have to demonstrate agility, adaptability and be quick on our feet to navigate complex and rapidly evolving market conditions.

The pharmaceutical market in Turkey boasts a solid infrastructure and is well regulated. While launching products, it is very important to understand the needs of your key stakeholders, specifically those of our governmental stakeholders. Closely understanding their requirements enables us to be ready to respond to requests or requirements and adapt our approach in case of environmental change and challenges. With this approach, we launched five new treatments in the past five years, with a strong pipeline of new indications and products on the way.
five years after the launch of Turkey’s localization policy, supporters of the move have tangible results to show for it. The policy, launched officially in 2016, required foreign producers to commit to localize the production of certain pharmaceutical products in Turkey or be exposed to exclusion from its social security system’s reimbursement scheme.

Those tangible results seem straightforward. One year prior to the policy announcement, made-in-Turkey pharmaceuticals had a 42 percent market share in terms of value, but overtook imported ones just three years later, in 2019, and today account for over 50 percent of the market.

In terms of physical infrastructure, the number of pharma production facilities went from 66 in 2015 to 96 in 2020 and, in the same five-year period, pharmaceutical production skyrocketed with a 52 percent increase, according to TurkStat.

It is no wonder then, that as a key stakeholder, Turkey’s Pharmaceutical Manufacturers Association (IEIS) deems the continuation of localization policies of great importance for the industry. “During this process, the industry invested in new technologies, increased capacity utilization and employment while imports diminished,” says secretary general Savas Malkoc.

While the local manufacturing industry and defenders of the policy celebrate the changes it has brought, official opponent of the policy, namely the European Union (EU), await a high-stakes final report by the World Trade Organization that could put an end to the policy and have global repercussions.

The Dispute

The EU – home to many pharma companies that have complied and invested in Turkish localization in recent years such as Boehringer Ingelheim, Bayer, Novo Nordisk, Recordati and Sanofi – alleges that the localization measures taken by Turkey, and its implicit request for technology transfer, fail to comply with four WTO agreements that all members are bound to follow.

The official complaint argues against three main aspects of the policy. First, that exclusion of non-localized products from the reimbursement scheme “significantly impairs” the competitive opportunities in the Turkish market. Second, that even when a product does comply with localization requirements, the country “bans” further importation of the product. And third, it argues that Turkey is prioritizing reimbursement applications of domestic products over imported ones, even for products that the country has not asked to be localized.

After Turkish and EU representatives failed to settle the dispute during consultations held in Geneva in May 2019, the EU requested the establishment of a panel of experts to adjudicate the merits of the case.

The EU is seemingly not alone in disagreeing with the policy as Switzerland, China, Japan, India, Russia, and the United States were included as “third parties” in the original complaint which provided them specific legal rights when it comes to participating in the dispute process.

Amongst that group, the US took a step forward one month before the failed Geneva consultations, requesting to join the consultations alleging that it had “substantial trade interests” in them, pointing to the USD
219 million worth of pharma products the country exported to Turkey in 2018.

As of the writing of this report (October 2021), stakeholders await the expert panel’s final report which, due to delays caused by the COVID-19 pandemic, is expected to be issued in the second half of 2021.

A party that loses a case in the WTO is supposed to follow the recommendations of the panel report. If it fails to do so, it must seek agreement or compensation with the winning party. If all fails, the WTO can authorize trade sanctions against the losing party.

As it awaits the resolution, IEIS maintains its support for Turkish localization. “The practice does not contradict international resolutions and conventions. From our perspective, the government should continue with the localization efforts to increase capacity, attract more foreign investment and technology,” Savas Malkoc says.

### HOW DOES THE WTO DISPUTE SETTLEMENT PROCESS WORK?

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<thead>
<tr>
<th>Phase</th>
<th>Description</th>
<th>Time</th>
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<tr>
<td>1. Request of consultation</td>
<td>The complaining party requests formal consultations with the other WTO member country involved in the dispute. The Dispute Settlement Body (DSB) administers the rules and procedures governing the dispute settlement process.</td>
<td>up to 60 days</td>
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<tr>
<td>2. Establishment of a panel of experts</td>
<td>If the consultations fail to resolve the problem, the complainant can request that the DSB establish a panel of experts to adjudicate the merits of the case. The panel process in many ways resembles a typical court case. Both parties to the dispute submit written briefs and present oral arguments before the panel.</td>
<td>up to 45 days.</td>
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<tr>
<td>3. Panel’s report</td>
<td>After hearing arguments from both sides and examining all the evidence, the panel issues a final report with findings and recommendations.</td>
<td>within 6 months of the start of proceedings</td>
</tr>
<tr>
<td>4.- Appeal</td>
<td>Appeals are heard by a separate group of experts, who then issue their own report with their own findings and recommendations.</td>
<td></td>
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<tr>
<td>5.- Compliance with the recommendations</td>
<td>A party that loses a case in the WTO is supposed to follow the recommendations of the panel report and is given a “reasonable period of time” to comply.</td>
<td>usually no longer than 15 months</td>
</tr>
<tr>
<td>6.- Consequences for non-compliance</td>
<td>If the losing party fails to comply with the recommendations, it must seek agreement or compensation. Compensation may be granted in a variety of ways (e.g., tariff reductions or the lifting of quotas on certain products). The DSB can authorize the winning party to apply equivalent trade sanctions against the losing party.</td>
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Biosimilars on the Rise

With an already well-established manufacturing industry for pharmaceuticals, Turkey has been aiming to move with global trends and invest in biologics production, specifically in biosimilars.

The share of biotechnological pharmaceuticals has reached 30 percent globally, a rate that is expected to continue increasing, but the market share in Turkey last year stood at just over 18 percent. There are currently 254 forms of originator biologics under 116 licensed brands in the country, according to IEIS, and 94 forms of biosimilars under 25 brands.

“According to recent reports, the main driving force for European markets will be biosimilars and Turkey has to get on front of that; we have the necessary facilities and capabilities because Turkish companies have been investing heavily in biosimilars,” asserts Savas Malkoc, secretary general of IEIS, whose latest report reveals that 29 types of biosimilars are being produced in Turkey.

Investment in the field by Turkish companies can be traced back over a decade, but competence remains a work in progress since the production of biologics uses specialized processes that do not always resemble facilities, machinery, or equipment used to produce chemical drugs. While the number of critical tests done in the manufacturing process of chemical drugs is between 40-50, for biologics it can take 250 or more.

“Volume is key in biosimilar production, but you also need the know-how because it is more complex than traditional manufacturing,” believes Güldem Berkman from Amgen – a company that is producing biosimilars for almost 80 countries from Turkey – and suggests that Turkish companies must export to global markets.

Philipp Haas from DEVA agrees, explaining that “there is a trend towards biosimilars in Turkey and companies are trying to develop them, but the penetration continues to be underwhelming and the market remains dominated by big multinational companies.”
Amongst those international companies already competing in the Turkish biosimilars market, Amgen, Celltrion and Viatris stand out. For those companies that joined the biosimilars train years ago on the local side, choosing the right corner is strategically vital.

“It is true that Turkish companies were slow to invest in biosimilars but, fortunately, we are targeting the products that will lose patent protection after 2026-28 so we can be on a level playing field,” says Hatice Öncel from Ilko Pharmaceuticals.

For Polifarma’s Chairman, Ufuk Kumrulu, the best path forward is one away from “highly known” molecules such as monoclonal antibodies in favor of niche biosimilars: “There are more than 200 registered monoclonal antibodies (mAbs) biosimilar products in Turkey, but there are several molecules that are not registered, and we intend to be the first ones to get them to the local market and some export markets.”

Standing out from the crowd is Arven Pharmaceuticals, a company whose biosimilars development and manufacturing process has been applauded but has decided to open them up to the rest of the industry as a CDMO after an unpleasant experience. “Two years ago, we invested in trastuzumab and bevacizumab, two monoclonal antibodies, which were ready for the scale up process and first clinical studies, but unfortunately the reimbursement system in Turkey made prices for those products too low for us to consider it a feasible investment,” recounts CEO Zafer Toksöz.

BIOTECHNOLOGICAL DRUGS (VALUE) (TRY, BILLION)

Source: IQVIA, IEIS

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Can you walk us through the peculiar backstory of Ilko Pharmaceuticals and its current place within the Turkish pharma landscape?

**HATICE ÖNCEL (HÖ):** Ilko Pharmaceuticals is a family-owned company. The Öncel family, which has been involved with the Turkish pharmaceutical industry for over five decades, used to operate another company but sold it in 2006 to a venture capital firm. After a period of non-competition, we re-invested in the sector through Ilko Pharmaceuticals which began commercial and manufacturing activities in 2012.

Our business strategy since the beginning has been to create a wide portfolio and, after examining the future of the industry, pivoted from a simple-generics-only approach to include differentiated products with advanced technologies such as controlled-release tablets. In 2015, the company opted to make a considerable investment in the biotech field through a joint venture with Genexine, a South Korean company. With them, we are developing biobetter products.

To support this investment, Ilko established its own biotech R&D centre through which it will enter clinical development of its pipeline at the end of this year. The rationale behind this investment is that the future of pharma will rely on biological value-added products as the strongest segment.

On top of that, we are gaining market share in the local market and increasing our export activities every year. We are present in three key diverse areas (value added generics, biotech, and consumer health products) and did it all in less than nine years since starting the company.

How supportive has the Turkish government been in your R&D efforts at a moment when they have emphasized the importance of clinical development to foster a globally competitive industry?

**HÖ:** We are currently running one project with the Scientific and Technological Research Council of Turkey (TUBITAK). The council is supporting three projects in the area and ours is one of them, a biosimilar program that has been conducive to obtaining R&D know-how.

Beyond that collaboration, we are developing a biobetter product with our South Korean partner and have sent applications to the Health Institutes of Turkey (TUSEB) for phase III clinical trials. If it succeeds, it will be our first biological product on the market.

For us, the strategy to commercialize the product internationally will be focused on a rapid penetration of regional countries and Europe, and the second stage will be an FDA application so we can enter the US market.

With the current challenges around pricing and the currency devaluation in Turkey, what is your strategy to find opportunities in the international markets?

**HÖ:** The biotech industry in Turkey is not large enough yet to recover your investment, so we are looking at export markets. In fact, 25 percent of our revenue is coming from abroad already, mostly from CIS countries, the Middle East and Africa.

We enjoy a competitive advantage since Turkish products are considered high-quality and less expensive than European pharma products. Penetrating the European market for Turkish companies is complex because, while it is stable, the margins are low; you can succeed with certain products such as biosimilars but not as much with generics.

It is true that Turkish companies were slow to invest in biosimilars but, fortunately, we are targeting the products that will lose patent protection after 2026-28 so we can be on a level playing field.
At the crossroads of Europe and Asia, Turkey’s geographical location has always been touted as a unique value proposition for companies looking to invest in the era of globalization. Many multinational companies across multiple sectors have chosen the country either as a manufacturing exporting base, such as Nestle, Sanofi, Amgen and Recordati, or as an administrative regional hub, like General Electric and GSK.

Turkey is “right in the centre of the Middle East and Europe, we have a superior geographical location that allows us to access different regions easily. There are direct flights to almost all countries in the area,” says Novo Norsk’s Burak Cem.

Turkey is an essential transport corridor, offering access to global trade routes by air, land and sea. Bordered by the Marmara, Black, Aegean and Mediterranean Seas, in addition to various land boarders, Turkey offers convenient access to Europe, Asia and North Africa.

That position has helped the country to secure a place as a regional logistics hub for pharmaceutical products. The sheer volume of imports and exports in serve as evidence; in 2020, a combined USD 5.1 billion worth of pharma products crossed Turkish borders.

At the center of that large-scale movement of pharma goods is often Turkish Cargo, the air cargo transportation operations of Turkish Airlines, which transports one out of every 20 pieces of air cargo carried throughout the world, according to World Air Cargo Data. Turkish Airlines prides itself on being the airline flying to the most countries in the world.

“Turkish Cargo transports healthcare to more than 300 destinations in the world with its operational quality and special transportation methods..., we transport sensitive medicine with a half-life of less than 24 hours, as to prevent them from losing their effectiveness for patients in West Asia, Africa, Eastern Europe, and India, and we deliver them throughout the world,” explains Turhan Özen, chief cargo officer for Turkish Airlines.

The company assures that pharmaceuticals “are privileged” with respect to the ramp services that are performed during loading and offloading of cargo. “Increasing its [global] market share in pharmaceutical transportation to eight percent, Turkish Cargo enhanced its capacity when it comes to cold air depots while increasing its active and passive container capacity in order to prioritize medical transportation,” says Özen.

In a product category with strict temperature requirements, Özen adds that “any cargo, which includes pharmaceutical products with high sensitivity to temperature, such as vaccines, insulin, and anti-cancer drugs is preserved at the conditions and capacities as requested by our customers.” Özen is also keen to foreground the significance of “va-Q-tainer,” a container they say is “perfect” for global transportation of clinical and pharma goods since it can provide 120 hours of performance without the need of recharging or re-icing. 😊
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We speak directly with healthcare leaders and pharmaceutical executives globally.