GLOBAL BUSINESS REPORTS

INDUSTRY EXPLORATIONS

TURKEY

PHARMACEUTICALS AND BIOPHARMACEUTICALS

2020

Pricing and Regulation - Domestic and Export Markets - Manufacturing Capability
Localization - Biopharmaceuticals - Industry-University Partnerships - Investment

Dear Reader,

Welcome to the *2020 Turkey Pharma and Biopharma* Report, a joint publication by GBR and IEIS, providing the most comprehensive study of Turkey's pharmaceuticals and biotechnology industry for the benefit of international and local stakeholders alike. The report will be distributed in Turkey as well as at CPhI and Bio Expo events around the world.

This last time that GBR took the pulse of the Turkish pharma market was in 2015, since when, plenty has changed. Turkey has been accepted in the PIC(S), has launched a controversial localisation policy, and also kick-started its biopharma sector. Today, Turkish executives speak about foreign markets alongside the domestic one. Biotech terms also entered the manufacturing vocabulary, as the industry bifurcated into a mature pharma sector and a nascent biopharma sector.

But the pharmaceuticals industry has not had an easy ride: healthcare spending has been on a downward path for a decade, despite rising medical costs; political events, including the coup attempt in 2016 and the war in Syria, sent ripple effects across different industries, including pharma. Despite these challenges, the Turkish pharmaceuticals industry nevertheless rose from the 16th to become the 14th largest in the world by market value, according to IMS Health rankings, and it is not ready to stop here. The government is determined to make Turkey a top 10 pharma hub by 2023, when the Republic celebrates its 100 years anniversary.

In recent years, public incentives have fuelled the growth of the industry, especially in developing the biotech sector, increasing exports and boosting R&D spending. GBR assesses whether these measures are sufficient and sustainable. Even if Turkey is only three years away from its centenary celebration, the pharma industry seems further distanced from realizing its goals.

It was unforeseen that 2020 would be marked by a pandemic that has shaken the course of life and business globally. The Turkish pharmaceuticals industry has suddenly to confront an unprecedented crisis, bringing pressure, urgency and a daunting mission to control the effects of the rapidly spreading virus. Dutifully supporting healthcare provision, the Turkish pharma sector braces for manifold disruptions, likely to manifest both in the short and long run. What these may entail is explored in our special article addressing the impact of COVID-19 in Turkey.

GBR's publications take a look at markets not through the distant lens of statistics and media clips, but by sending expert eyes on the ground. GBR reporters spent two months in the heart of Istanbul, the hub of Turkish pharmaceuticals, meeting face to face with the industry's leaders and its varied stakeholders. With this occasion, we would like to thank each of the contributors who took the time to meet with the team and discuss the industry's intricacies, contradictions and its unfathomed opportunities.

We wish you an enjoyable read!

Alice Pascoletti
Managing Director
Global Business Reports

Turgut Tokgöz
Secretary General
IEIS

Editorial Analysis

GBR journalists provide unique and first-hand analysis into all aspects of the Turkish pharma and biopharma industry after months on the ground

8, 22, 38, 52, 74, 88...

Exclusive Interviews

Leading industry figures share their thoughts on aspects such as price control, localisation, or exports strategies

13, 15, 26, 45, 54, 83, 91...

Industry Views

The key industry executives and opinion-formers are put in conversation on the most topical issues affecting the industry

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Turkey

TURKEY PHARMACEUTICALS & BIOPHARMACEUTICALS 2020
Industry Explorations
Global Business Reports

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Edited by Mungo Smith
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A Global Business Reports Publication
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INTRODUCTION TO TURKISH PHARMACEUTICALS AND BIOPHARMACEUTICALS

» The Turkish pharma industry continues to assert its global presence despite being heavily burdened by the fluctuating price regulations in its local environment. «

- İsmail Yormaz,
General Manager,
Recordati İlaç

Image courtesy of AstraZeneca

Image courtesy of Drogsan

A West–Meets–East of the Pharma Industry

PORTRAIT OF THE INDUSTRY

In the offices of pharmaceutical companies across Istanbul, a portrait of the father of the Turkish Republic, Mustafa Kemal Atatürk, who engineered the transformation of Turkey into a modern nation state, hangs upon the wall. He is a suitable figure to watch over an industry that seeks to modernize and reinvent itself. With three years left until the centenary of the country's creation, Turkey has ambitious plans to prove itself as a competitive economy on the international stage and the pharmaceuticals industry has been identified to play a lead role. As set out in the government's Vision 2023, Turkey aims to become one of the top ten worldwide largest economies in health services.

The Turkish pharma industry is presently the 14th largest by value in the world, having moved up three positions over the last five years in IMS rankings. Out of the US$1.2 trillion estimated value of the global pharmaceuticals industry, the Turkish industry represents almost US$6 billion (40.7 billion TL). The sector is characterized by a unique mix of high quality and low prices, a paradox achieved by a combination of tough international market standards and stringent domestic price controls.

Since the launch of the Healthcare Transformation Program in 2003, the government assures free healthcare coverage to 95% of the population. In taking the healthcare of the population under its responsibility, the government shifted part of this burden to industry, as the healthcare transformation program of 2003 included a reference price system to control the price of drugs and keep in check public spending on healthcare. The pressure stemming from this high-quality-low-price conundrum has led to the creation of a resilient industry, but one that has learned to prioritize survival before growth. Turkish pharmaceutical companies are currently running at half of their manufacturing capacity and, moreover, the drugs produced are primarily low-value generics while almost all originator drugs, as well as vaccines, blood products, biologicals and biosimilars are imported. Given this significant dependence on imports, internal market pressures are doubled by external price pressures. The macroeconomic volatility of the country has kept the pulse of the industry at a low pace and the economy crisis of 2018 stalled it further.

The future of Turkey's pharmaceutical industry will largely depend on its ability to take advantage of a recent government impetus to develop the sector. The government's incentives include increasing local production by rolling out a localization policy, ramping up exports to reduce the trade deficit, as well as developing the country's biopharma sector. The focus on the pharma sector is partly due to its importance as the third largest contributor to Turkey's trade deficit and to its potential to secure the domestic supply of medicines. With the interests of both the government and the industry approaching a convergence, the industry is bound to experience transformative shifts as it enters the 2020s.

Evolution of the market

The Turkish pharma industry is mature, but it is only in the last decade that the market has migrated from a low-margin, mass generics model to chronic therapies and biologics in a trend that aspires higher-value products. In the last 10 years, 200 new companies forced their entry into the generics market at a time when the government gave away generous incentives to kick-start a biotech sector. With increased competition in generics put in contrast to promising prospects in biopharma, the pharmaceuticals market is evolving to incorporate the prefix "bio" wherever possible. Atabay, a well-known leader in paracetamol, is an example: Just as the third generation took the helm of the company, investments in biopharma began.

While biopharma is gaining significant momentum, 80% of prescriptions remain in the domain of classical drugs. In this segment, the maturation of the product portfolios bears the signs of

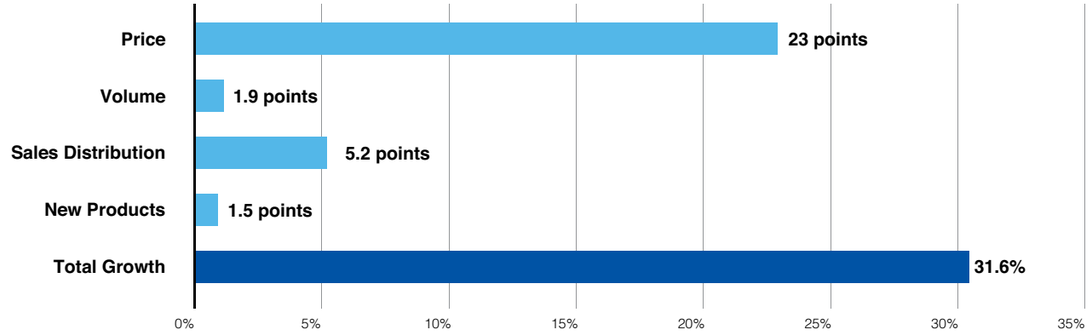
Image courtesy of Abdi Ibrahim

an industry overstretched by low prices and competition. Even if one in seven Turkish pharma companies is a local player, it is the foreign players that take 69% of market share by value. With multinationals like Sanofi claiming the leadership in popular chronic segments like CNS or cardiovascular disease, local players choose the niche therapies in which they stand a better chance of grabbing the first generic – the front line in the battle for the generics market. The localization policy introduced by the government in 2016 aims to give local players the upper hand by obliging all multinationals with products destined for Turkey to produce these products locally. This has led to more interaction between local and foreign players and a rise in collaborations for contract manufacturing. New companies and CMOs are already bracing for increased demand in different product categories. Regardless of the localization policy, a broader tendency has been to invest in difficult-to-make generics, like injectables or new radiopharmaceuticals.

Turkish pharma has evolved according to the challenges posed by the industry; however, the success of any strategy is conditioned by the pricing system, which is a constant point of return. In order to diversify the product basket or be competitive with a first or super generic, R&D efforts need to be commensurate. If increasing the product basket proves insufficient and companies instead look to increase the basket of countries they seek to operate in, profits in the domestic markets need to be lucrative to sustain expansion. The biopharma sector brings hope at the top of the pyramid for high-value products, but this is a capital-intensive sector sitting at odds with the cost-saving mentality that the industry has been forced to adopt. Besides finding the repertoire of drugs that can propel Turkey into world markets, as well as effectively responding to the needs of its 83 million population, Turkish companies are yet to make big strides to evolve from their current status. Perhaps it will take another decade or more before its model of growth will be proven right or wrong. ■

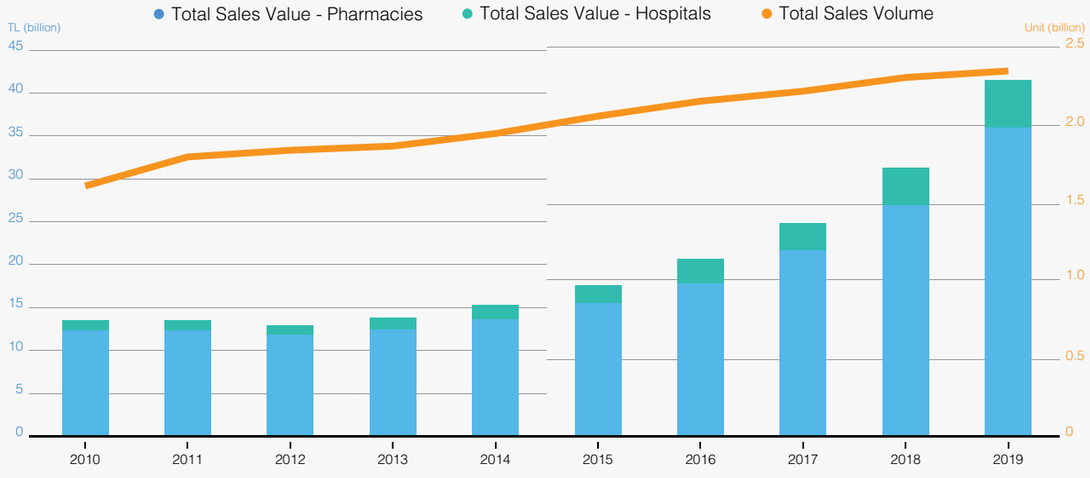
SOURCES OF GROWTH

Source: IQVIA, İEİS



TURKISH PHARMACEUTICAL MARKET

Source: IQVIA, İEİS



BREAKDOWN OF THE PHARMACEUTICAL MARKET

Source: IQVIA, İEİS

	2010		2019	
	Value (Billion TL)	Share	Value (Billion TL)	Share
Drug	**13.39**	**100%**	**40,72**	**100,0%**
Prescription	**13.35**	**99.7%**	**40,55**	**99,6%**
Reimbursed	13.02	97.2%	39,01	95,8%
Non-reimbursed	0.33	2.5%	1,54	3,8%
Non-prescription	**0.05**	**0.3%**	**0,18**	**0,4%**
Reimbursed	0.02	0.2%	0,05	0,1%
Non-reimbursed	0.02	0.2%	0,12	0,3%

Message from TÜBİTAK

Prof. Dr. Hasan Mandal
Acting President, Presidency of the Republic of Turkey Science,
Technology and Innovation Policy Council (TÜBİTAK)

Dear Reader,

The pharmaceutical industry has an important role in supporting opportunities for a healthier society. In Turkey, R&D and innovation activities in pharmaceuticals and biopharmaceuticals are of prime importance. The Eleventh Development Plan, that covers the years 2019-2023 leading to the 100th anniversary of Turkey, designates medicine and biomedical equipment as one of the prioritized sectors while also underlining the vital importance of biotechnological drugs.

The importance of biotechnological drugs is further underlined by one of the policy boards of the Presidency of the Republic of Turkey, namely the Science, Technology and Innovation Policy Council, of which I serve as acting president. The results of a comprehensive technology area evaluation and prioritization study determined the priority of biotechnological drug technologies. The framework was based on two dimensions on impact and feasibility with sub-dimensions and indicators. Among 27 technology areas, biotechnological drug technologies were one of the 11 technology areas with the highest impact and feasibility. Impact is based on a combined view of economic, societal and national security impacts. Feasibility represents knowledge and technological accumulation in publications, projects and patents, research infrastructure, qualified human resources, access to financial capital, and the technology readiness level in our country. Currently, the pharmaceutical industry is one of the most active stakeholders within the new co-creation platforms that are implemented by the Scientific and Technological Research Council of Turkey (TÜBİTAK). These involve specialized technology hubs that are centered on research infrastructures as well as industrial innovation hubs that are centered on big firms. These new structures are based on the phased support of the Centers of Excellence Support Program High Technology Platforms Call and the Industry Innovation Networks Mechanism for increasing systematic flows of knowledge throughout the value chain. Here, the pharmaceutical industry is taking a leading role based on targeted scientific and technological specialization in the life sciences and health biotechnology, biotechnological drugs and vaccines, and nanotechnology.

Both large firms and SMEs from the pharmaceutical ecosystem are further partnering with universities for qualified human resource development through university-industry co-creation. The mission-oriented Industrial Doctorate Program forges ties between sectors to build critical mass in targeted areas with continued support for employment opportunities after graduation. In addition, most of the research infrastructures that have been certified under Law 6550 on Supporting Research Infrastructures are active in the fields of life sciences, biomedicine and genetics. The Turkish pharmaceutical industry is merging disciplines in knowledge production in line with multidisciplinary developments.

From scientific excellence to partnerships, the Turkish pharmaceutical industry is aligned with the R&D value chains of tomorrow that will involve much more specialization and partnerships from target discovery, lead discovery, pre-clinical, clinical trials, filing, and market launch. In this respect, partnerships between industry, academia, research institutes, hospitals, diagnostic, and innovation alliances and networks that are rising on the global scene have equivalences in the Turkish ecosystem. These key developments will be sustained with continued support to the pharmaceutical industry, including through the call program of TÜBİTAK in the field of health that includes calls on discovery of new molecules, biotechnological drugs, and biosimilars. The call program specifies technology readiness levels and expectations on partner compositions.

Our outlook for the Turkish biotechnological drug industry is bright based on the competences and dynamism of the ecosystem's actors. Based on WIPO statistics, Turkey is among the fastest growing emerging economies in pharmaceutical related patent publications in recent years with a compound growth rate of 11.7%. [1]According to the R&D survey by the Turkish Statistical Institute, there were close to 1,500 full-time equivalent researchers with roles in basic pharmaceutical product manufacturing and pharmaceutical preparations in the private sector. Researchers in this field also had one of the highest graduate researcher shares in total researchers within the manufacturing sector. Based on the same survey, medical sciences and natural sciences constituted 41% of the total R&D expenditure of higher education institutes.

All ecosystem actors that have a role in positioning Turkey as an efficient hub for qualified human resources and knowledge production in the pharmaceutical and biotechnological drug industry are warmly acknowledged. Special appreciation is given to the Pharmaceutical Manufacturers Association of Turkey for their efforts that includes this valuable publication. I further express my confidence in the continued success of the co-production in this industry. Together with their success, we will achieve impact towards increasing healthy lifespans.

[1] Global Innovation Index: Creating Healthy Lives - The Future of Medical Innovation, 2019.

Dr. Hakkı Gürsöz

President
TİTCK
Turkish Medicines and
Medical Devices Agency

An analysis of the pharmaceutical regulators and pharmaceutical industries of various countries across the world reveals the following: The more competent the pharmaceutical regulator is in a country, the more developed is the pharmaceutical industry.

What are Turkish Medicines and Medical Devices Agency's (TİTCK) efforts for advancing the pharmaceutical industry and turning Turkey into a manufacturing base?

The aim here is to shift to a manufacturing structure which can produce high value added products, deliver these products and services to global markets, and meet a greater portion of the domestic demand for pharmaceuticals and medical devices. In this context, since 2016, a number of incentive mechanisms have been established in all segments of the public sector in order to encourage domestic production, especially the prioritization in TİTCK's licensing processes. Since then, 22 new pharmaceutical and radiopharmaceutical facilities have been inaugurated. At the moment, Turkey is home to 86 pharmaceutical production facilities, 10 radiopharmaceutical production facilities (pharmaceuticals used in imaging), 12 raw material production facilities, 8 advanced treatment medical production facilities, 1 special medical dietary nutrition facility, 2 traditional herbal medicine production facilities, 94 medical gas facilities and 46 secondary packaging facilities, which add up to a total of 259 domestic production facilities. The percentage of local products in the pharmaceuticals consumed in our country has risen to 83% in terms of units. In terms of value, the percentage has gone up from 42% in 2016 to 51%.

Together with our pharmaceutical industry, we are working on a new incentive mechanism to further improve these percentages. At the core of this mechanism is an assessment based not only on localization but other criteria as well. Our work has reached a certain stage, and we will soon share it with our stakeholders.

At TİTCK you have been making remarkable progress in terms of collaborations with international organizations. What are the latest developments in this context?

An analysis of the pharmaceutical regulators and pharmaceutical industries of various countries across the world reveals the following: The more competent the pharmaceutical regulator is in a country, the more developed is the pharmaceutical industry. Therefore, while designating for ourselves the vision we have mentioned above, we also put forth a target for our industry. As for what has been achieved since 2012 in this context, we have first of all completed the PIC/S process, becoming a full member at the beginning of 2018. Immediately after that, we filed applications for full membership to ICH, and to join WHO's Listed Authorities. We currently have observer member status in the ICH. Since we meet all the criteria for full membership, we expect that our full membership will be announced in the first ICH Assembly of 2020. On the WHO side, we are furthering the process in accordance with a calendar of approximately three years.

What is the export potential of Turkey's pharmaceutical industry? What are TİTCK's activities to promote exports?

Turkey has a huge advantage in accessing many parts of the world thanks to its geographic location. The clearest indication of this is the fact that our products are exported to over 150 countries. We can clearly observe this advantage in the projects that global companies intend to implement in our country.

Our pharmaceutical exports have easily exceeded the US$1 billion threshold in the past few years. This was an important threshold for us, but it is now time to set new goals, because our true potential is far beyond that. Turkey already boasts world-class infrastructure and capacity in pharmaceutical production. We don't have any shortcomings in this regard. Furthermore, Turkey has a well-developed generics market. The generics will reduce the burden of health expenditure on public finance, while also increasing export potential thanks to their competitive edge.

At TİTCK, we strive to fulfill our responsibility in increasing exports. For example, we give priority to the products designated as export priorities and quickly obtain licenses for them. Likewise, a natural result of the aforementioned processes that we carry out together with international organizations will be a surge in exports. We shall eliminate all doubts about the quality, safety and efficiency of the products licensed in Turkey. Our aim is to ensure that the products licensed by TİTCK are fully trusted across the world. ■

IEIS
PHARMACEUTICAL MANUFACTURERS ASSOCIATION OF TURKEY
www.ieis.org.tr

Turkish Biopharmaceuticals Platform
www.biopharma.org.tr

Nezih Barut
Chairman,
Pharmaceutical Manufacturers Association of Turkey

As the Chairman of the Pharmaceutical Manufacturers Association of Turkey (IEIS), I am very pleased to reach out to you through this extensive report that portrays the Turkish pharmaceutical industry's state-of-the-art manufacturing capacity as well as its ongoing efforts to become a leading player in the biotechnology field.

Our pharmaceutical industry is one of the most rooted, dynamic and strategic sectors in Turkey. With 83 pharmaceutical and 11 raw material facilities that meet international manufacturing standards as well as 34 accredited R&D centers, and counting approximately 38,000 employees, our industry caters to our growing and aging population with over 12,000 products. Locally produced products currently make up 87% and 52% of the market in terms of volume and value, respectively.

Our manufacturing facilities outperform their counterparts in the developed world; a token of how the Turkish pharmaceutical industry has made headway, of which we can be proud. Our facilities manufacture cutting edge products with high added-value and we also accommodate multinational companies with long-term production contracts.

Our facilities undergo regular inspections by the Turkish Ministry of Health and are accredited by international authorities. Turkey was granted membership of the Pharmaceutical Inspection Co-operation Scheme (PIC/S) in 2018, which testifies to our world-class inspection and pharmaceutical manufacturing standards.

One of our primary goals of IEIS is to make our country a global pharmaceutical manufacturing hub. Within this context, we fully support the localization initiatives carried out by the Turkish Ministry of Health. This policy has produced tangible positive results for our industry. Our manufacturing technologies have been upgraded, capacity utilization has dramatically increased and employment is on the rise.

Another major outcome of this policy is the positive impact on foreign trade figures. Imports growth has stopped while long-term contract manufacturing agreements, that also incorporate exports of some products, have been supporting our strong exports growth.

On the biotechnology front, IEIS established the Turkish Biopharmaceuticals Platform at the end of 2016. It works as a synergy-driven networking and coordination platform with the participation of companies that are active in this field. We undertook large-scale investments with a long-term perspective in this field. There are now R&D and manufacturing capacities available and soon we will accumulate the fruits from these investments. Efforts are underway for manufacturing two reference biotechnological drugs and 40 biosimilars by in Turkey by 2024.

This journey will not be without its challenges and shortcomings, but we are confident that if we can develop a robust and functional public-academy-industry cooperation, we will earn a place among the leading biotech players.

Turkish public authorities have taken significant steps supporting our efforts. Remarkable improvements have been made in R&D regulations over the past couple of years. We have also seen some very instrumental incentives in the field of biotechnology. Yet, we also need a friendly regulatory climate that favors biosimilars and supports our initiatives.

The legislation governing this field must be local and science based. We need to be able to produce quality products in a timely manner to be able to remain competitive in the global market. Thus, the licensing process for biosimilar products should be improved. We also need an-efficient and well-designed incentive system that is geared towards product development.

Another key to success in this field is a qualified workforce. As our efforts grow, so do our needs for qualified human resources. Our major expectation from our universities is to educate scientists to collaborate with. With this vision in mind, we are in close contact and cooperation with our universities.

On a final note, I would like to mention our industry's strong exports performance. Pharmaceutical exports have been outgrowing Turkey's total exports. In 2019, we expect pharmaceutical exports to reach US$1.25 billion. We export our medicines to 170 destinations.

As IEIS, we will pursue our dedicated efforts with a vision centered around R&D, biotechnology, manufacturing, employment, and exports. We wholeheartedly believe that we will take our industry to the next level in cooperation with all the public institutions, national and multinational companies, academic research organizations and other stakeholders featured in this report.

We are pleased to present this report to the readers with the hope that it will provide a wide window into the Turkish pharmaceutical industry's capacity, strength and goals.

SPECIAL ARTICLE

Impact of COVID–19 in Turkey

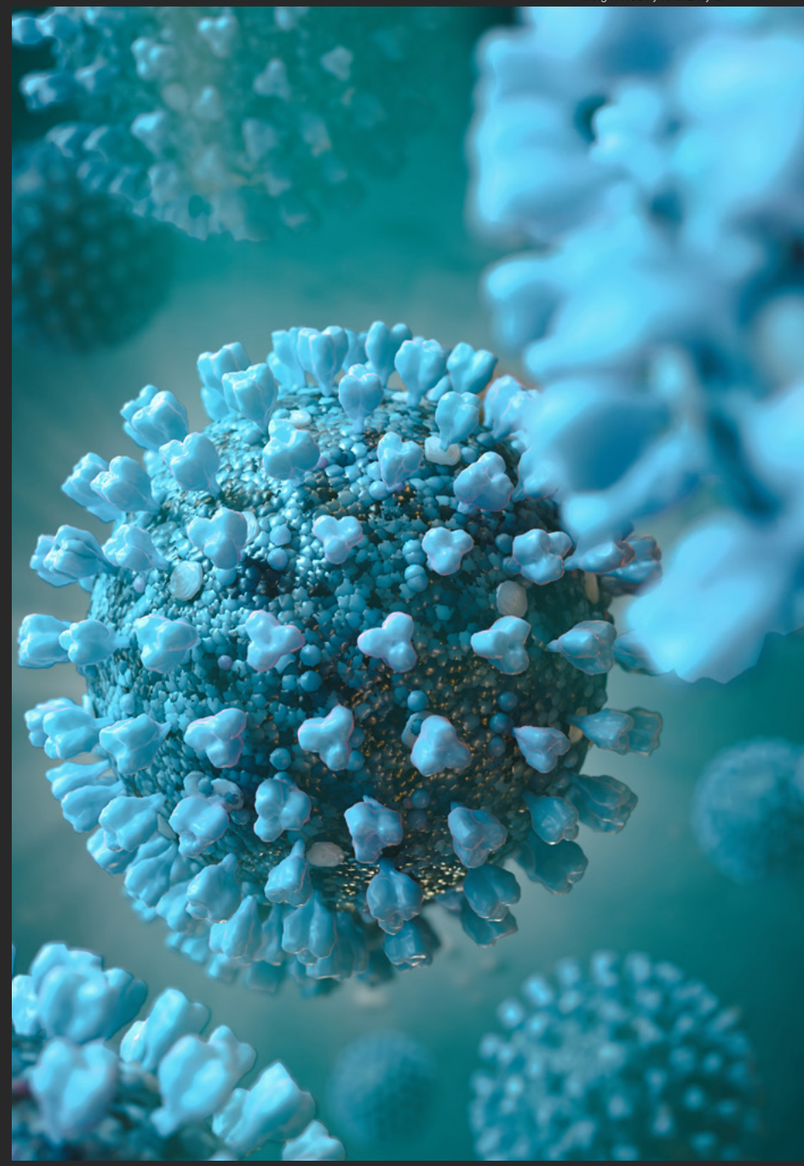
SUMMARY

15 April 2020: GBR books are designed to rest on the desks of our readers for over a year, as we look at the long-term view of the market and analyze its trends. Unforeseen events, such as the deadly COVID-19 pandemic that is currently disrupting society, throw everything into a new perspective. This article has been added to the original research in mid-April 2020, approximately a month after the first COVID-19 case was confirmed in Turkey. These special circumstances dictate that the government's response and the industry's involvement will have broader implications for future health policy, at a time when the balancing act between the country's economic vision and its tight social spending has never been more delicate.

Overview of the outbreak

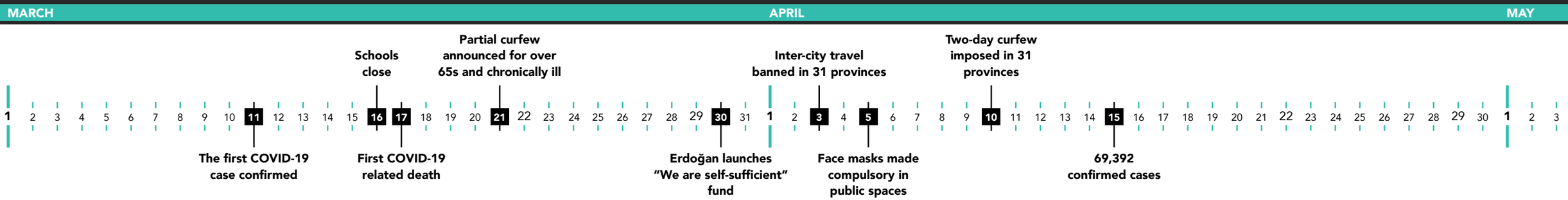
First described as a "pneumonia of unknown cause" and compared to the SARS virus of 2003, the flu-like virus born in the Chinese city of Wuhan eventually became recognized as COVID-19 or coronavirus. On the 31st of December, the World Health Organization (WHO) was notified of the existence of the virus and, a month later, the organization declared the outbreak a public health emergency. At the moment of writing, over 2 million people across 212 countries have tested positive and more than 134,286 have died.
Turkey was the last major economy with a population of over 50 million people free of the virus until 11th of March, when the first case was confirmed, at a time when most of Europe, the United States, Iran and China itself were either reaching towards or overcoming the peak of the epidemic. As of 15 of April, Turkey has registered over 69,392 cases of COVID 19, among which 1,518 fatalities and 5,674 recovered.
The epicenter of the outbreak is Istanbul, the largest city, where 60% of all cases are found. On account of the country's youthful demographic, incidences of virus-related deaths among Turkey's under-60 patients are higher than in other countries: 25% of the first 356 deaths occurred in this age group. Turkey reportedly runs more than 20,000 tests a day. By April 4th, 181,445 tests had been done in the country.
Turkey's public response to the virus
Taking note of what Turkey criticized as lax measures taken in some European countries, Turkish authorities immediately imposed restrictions on travel and public gatherings. By the end of March, all international passenger flights had been suspended; coming to April, the President announced a 15-days ban on vehicles leaving or entering 31 provinces. People aged under 20 and over 65 continue to be prohibited from leaving their homes unless proven necessary, which means 30% of the population is under curfew. However, the restrictions for people outside of these age brackets are much more lenient. Working age people are recommended to go into voluntary isolation, but they are not enforced to do so. There is also little financial aid for those choosing to stay at home, which forces many to continue working. Unionists and opposition leaders claim that firmer measures should be enforced to protect workers from contagion. Turkey has so far also resisted calls for a lockdown and only ordered national isolation on the 10th of April, when the authorities ordered a two-day curfew over the weekend. The order backfired because it was announced just hours before it was due to become active, and unprepared people crowded to the shops to make provisions for the weekend. The chaos that ensued caused Turkey's popular minister of the Interior to resign, though the President predictably refused to accept his resignation.
Public figures indicate that the rate of new infections has dropped to 15.9% in April, down by 10 percentage points from the previous month, but international media suggest that the rate of spread of over 4,000 a day is one of the fastest in the world. Prof. Dr. Berrin Erdag, a representative of the GEBI research center within state-agency TÜBİTAK, is optimistic about the actions taken to date: "We believe that the coronavirus is not stronger than the precautions that will be taken."
Having experienced a difficult economic crisis in 2018, Turkey is trying to overcome the epidemic without endangering its perilous economic recovery, which is why it hesitates to order a close-down, and cannot subsidize the salaries of those in isolation. Turkey's economy posted growth of 0.9% in 2019, according to TurkStat, but was poised for robust growth of 6% in 2020. With dashed hopes for a propitious 2020, Turkey's economy will experience a sharp contraction this year. Besides the energy sector, which will save Turkey US$12 billion in energy imports due to the collapsed oil prices, all other economic sectors are expected to be negatively affected.
The government allocated a rescue package of 100 billion lira (US$15 billion) to mitigate the slowdown, as well as allowing for the postponement of debt payments and a reduction in corporate taxes. Businesses are also helped with a three-year loan at fixed interest rates and six months repayment window. Turkey's moderate debt of around 30% of its GDP allows it to sustain further borrowing. However, the caveat of Turkey's economic recovery is that it remains strongly tied to the recovery of other countries. Economists have compared the unprecedented speed with which economies have shut down with the effects triggered by the fall of an asteroid. According to the Economist Intelligence Unit (EIU), the global economy will retract by 2.5% in 2020, which is a deeper recession than that experienced during the financial crisis of 2008.

Image courtesy of dottedyeti



Consequences of COVID-19 for the pharma industry

In times like these, the pharmaceutical sector is complexly affected, not only as an industry suffering from the general economic downturn and disruption of the supply chain, but also in its capacity as a key supplier of medicines to hospitals. Uniquely, the pharma industry is looked upon for its research ability in the direct fight against the novel virus. Pharma companies also bear a responsibility towards their workers. In view of these considerations, it is not surprising to see that 95% of global pharma executives surveyed are concerned about the impact of COVID-19, based on the European Pharmaceutical Review.
Turkey's pharmaceuticals sector is not exempted from any of these pressures. "The COVID-19 outbreak brought to focus the need for a strong healthcare system and pharmaceutical industry. The Turkish pharmaceutical industry has a long-standing culture of production, which is vital in the current outbreak," said Turgut Togsöz, Secretary General of IEIS.
Many will consider the pharmaceuticals sector to enjoy a place of near impunity during a global health crisis, with some product demand even spiking at such times, but this is a simplistic take. Since the beginning of the outbreak, product demand has reeled out of its usual patterns. Antibiotics, antivirals, sedatives, IV fluids, as well as masks and medical devices like ventilators and testing kits, have been particularly sought after. In Turkey, the products which made the "Critical Product List" include muscle relaxants, blood pressure suppressors, antibiotics, analgesics, antibacterials, sedatives and others. Depending on each manufacturer's focus, some companies were more prepared to respond to the growing demand in these categories. Sterile injectable producer Tüm Ekip has 32 products within this guide, of



which 12 are considered of top priority. "At Tüm Ekip we are in the most crucial sector, since injectables have become even more important due to the higher rates of hospitalization. We are supporting all the hospitals in Turkey and many in the world for the treatment of infected patients," said Ahmet Altuğ Oğuz, CEO of Tüm Ekip.

More commonly, though, local producers have adapted their production lines to fit the demand. Local manufacturer Atabay has increased the production of paracetamol and antiviral oseltamivir, both used to alleviate symptoms and complications in cases of influenza. Turkish manufacturer Birgi Mefar has also boosted its line of primary products to meet the needs of the country's hospitals: "Birgi Mefar group continues its production by giving priority to products that are important in the pandemic treatment and we are planning in line with community needs," said Faik Somer, CEO of Birgi Mefar group.

Outside the range of these products, however, demand for medicines not related to the COVID-19 virus has dropped due to the fact that patients neglect or delay their usual treatments to avoid contact with hospitals, which are considered hotbeds for the spread. "Focusing on the combat with COVID-19, the pharmaceutical activity has slowed down relatively, which has led to a contraction of the pharmaceutical market," explained Philipp Haas, CEO and chairman of Deva Holding, a provider of a broad range of generics.

A more universal worry is caused by supply disruption in APIs due to production and shipping restrictions, explained Haas: "Supply of raw materials from Asia has become more difficult as production has slowed down in these hubs and even transportation is difficult to find. Deva has so far been able to provide the market with all its products and has taken every possible precaution to be able to do so in the future."

Like the United States and other pharma hubs, Turkey imports most of its raw materials from India and China. While India entered nationwide lockdown on the 25th of March, China has recently lifted the 11-week lockdown, hoping to gradually resume production across its different industrial sectors. At present, most manufacturers of formulations rely on stockpiles to last for about six months, which is industry practice. They are also required to report potential shortages in drug supply, should this become the case. Even so, it is too early to comment on when global supply networks will be restored to normality, and harder to speculate whether the threat of a cut-back on APIs from the East could lead to more investment in Western API production. At the very least, the issue of API-dependency is likely to receive renewed attention.

Lastly, the pharmaceutical sector is not immune to the inevitable economic slowdown that COVID-19 will cause. Recordati, an Italian-based company that entered the Turkish market in 2008, has already seen losses in its share prices. Listed on the Italian Stock Exchange, Recordati enjoyed steady growth until 19th February, when share prices started to drop, hitting the lowest on the 12th March after Italy's announcement of continued lockdown. For most private companies it is possible they will experience setbacks in their R&D programs. The biopharma space is likely to take a harsher hit than classic pharma since it is more dependent on both governmental and foreign investment.

The role of the pharmaceutical industry in fighting the pandemic

That the pharmaceutical industry falls under the category of "essential business" is an understatement in the current climate. The global pharmaceutical industry has a key role in helping nations and individuals to fight the pandemic through developing tests, treatments and vaccines. If until now the consequences on the pharma industry were principally discussed under a business imperative, the rest of this article deals with the special status of pharma companies. How the pharma industry is regarded and regulated after the pandemic will not be indifferent to the ways the industry players today engage with governments, with universities and with each other, nor to the ways they engage their own resources, especially when it comes to the science deployed in this period.

Ever since the local outbreak mutated into a pandemic, making it clear that the crisis was not one country's problem, the spirit of the scientific community has been one of cooperation. This sentiment was confirmed by the CEOs of top leading biopharma companies during the digital conference held by the International Federation of Pharmaceutical Manufacturers and Associations. Seeking to outrun the speed of the spread, scientific inquiry traveled rapidly between countries.

Private companies and research institutions from all corners of the world are working on developing a vaccine to immunize the population. Names such as Janssen, Sanofi, Zydus Cadila, Novavox, together with the University of Hong Kong, the University of Oxford or the University of Pittsburgh have each put candidate vaccines in pre-clinical studies. Beijing Institute of Biotechnology and Moderna/NIAID, as well as Sanofi have advanced their candidates to Phase 1 clinical studies. Despite the global effort dedicated to developing a vaccine, it will take at least another 12 months before a vaccine formula is approved; this will be followed by the challenge of running a campaign of production and immunization on a global scale - an endeavor likely to bring more opportunities for collaboration.

Besides vaccines, R&D departments around the world are also studying medicines to ameliorate symptoms and treat complications. The common route taken by most research laboratories has been to repurpose existing, already accepted therapies and trialing out their efficiency in COVID-19 cases. WHO's 10 countries mega-trial called "Solidarity" is testing out remdesivir, the antiviral originally designed to treat ebola. Ritonavir and lopinavir used normally in HIV patients is also tested to see if it can inhibit enzymes that the virus uses to replicate. Malaria treatments chloroquine and hydroxychloroquine have received the most attention, as the U.S. FDA approved their use, backed up by President Trump confident public endorsements, while the European EMA limited the medicines' use to clinical trials only. Until now, however, there is insufficient data to evidence the arbitrary efficiency of any of these drugs in COVID-19 cases. Filtering through the feedback received in other countries, Turkey is itself trialing these medicines to treat its patients. Koçak Pharma donated 10,000 packs of azithromycin, an antibiotic hypothesized to work in combination with hydroxychloroquine in the combat of COVID-19: "We are contributing to the battle against COVID-19 with products already in use such as azithromycin tablet as well as registering hydroxychloroquine tablet and oseltamivir capsules which are used in first-line treatment of COVID 19," said Hakan Koçak, CEO of Koçak Pharma.

Biomedicines, including plasma therapy and the use of monoclonal antibodies, are also hoped to create an autoimmune defense against the virus. The Turkish Red Crescent, for instance, is assessing the use of plasma therapy, or the transfusion of antibodies from recovered patients to new patients, for the treatment of COVID-19. Koçak Pharma is working on an active vaccine and hyperimmune serum in the same scope.

Going a step further into the chain, Atabay is bringing to speed API production for COVID-19 treatments: "Atabay's vigorous R&D work focuses on developing the API and the FDF to produce anti-viral drugs against the pandemic. In extraordinary times, having the expertise to produce both the API and the FDF makes the difference," said Doğan Taşkent, board member at Atabay İlaç.

These efforts are already yielding results across the board. Top pharma producer Abdi Ibrahim has presented the Ministry of Health with the first batch for a drug which has shown positive results in COVID-19 cases; the company vouched to donate this year's production to the government, starting with 1.6 million tablets in April. "We are utilizing all our resources to put an end to the threat facing our nation. As a company measuring its value by the contributions it makes to Turkey and the Turkish people, it is Abdi İbrahim's greatest wish that both the world and our country will emerge victorious from this crisis with as few losses as possible," stated Nezih Barut, chairman of Abdi Ibrahim, in a press release.

Overall, Turkish pharma companies have stepped up to demonstrate the resourcefulness of the national sector and their commitment to helping Turkey traverse this testing time. Recordati alone donated 1.1 million Turkish lira to the COVID-19 fund opened by President Erdoğan. Recordati Group vice president İsmail Yormaz said: "We have been looking into how we can best support our healthcare professionals and our people since the beginning of the pandemic. Recordati continues the production of all our products, maintaining high quality and hygiene while looking after our workers who have shown heroic determination during these times".

Balancing out the need for continued production with the health and safety of their employees, pharma companies need to keep up exemplary safety controls to further minimize contamination risks. "At Atabay, our first and utmost responsibility is towards our employees while working at full capacity," said Zeynep Atabay, owner of Atabay İlaç. ■

DOMESTIC MARKET

» Our pharmaceutical industry is one of the most rooted, dynamic and strategic sectors in Turkey. Our manufacturing facilities outperform their counterparts in the developed world, and the legislation governing this field must be local and science based. «

- Nezih Barut,
Chairman,
Pharmaceutical Manufacturers Association of Turkey (IEIS)

Image courtesy of Florabio

Image courtesy of Abdi İbrahim

The Domestic Market

LOW PRICES IN HIGH NUMBERS

Unforgiving price control

The domestic market for Turkey's pharmaceuticals industry is defined by challenging factors both in terms of pricing restrictions and instability in the political and economic landscape, but the demographic makeup of the country, together with increasing governmental industry support, is counteracting these unfavorable conditions. The healthcare industry has become an important component in both economics and politics: with the introduction of the Healthcare System, the government strengthened its popularity with the electorate to the detriment of the industry and, indirectly, the economy through the high costs of implementing such a system.

Prior to 2003, the system through which drugs were reimbursed to patients was largely inefficient and fragmented into separate packages by demographic segment. However, the introduction of the Healthcare Transformation Program brought different healthcare providers, including the Ministry of Health (MoH), Social Security Organization (SSK) and the private sector under the same umbrella. After streamlining health provision, the second stage was the introduction of the UHI Law (Universal Healthcare Insurance), which brought free coverage to all legal residents. With increased demand, more medical facilities and staff were put in place and medical infrastructure was improved significantly.

To sustain these costs, the price burden was passed to the industry. The government brought drug prices down to the lowest in Europe by enforcing a price reference system through which the cost of a Turkish drug is equivalent to the lowest out of five European countries: Greece, Portugal, Spain, Italy and France. On top of this measure, the prices of both generic and innovative drugs are subjected to "mandatory discounts," fixing the value of the Turkish Lira against the Euro at almost half the figure of its real market value. Currently, the conversion rate is set at 3.40 TL for one euro, while the market rate is 6.56 TL. Up until 2015, the conversion was fixed at 1.95 TL, before a legal trial decided in favor of the industry and the rate was relaxed to its current figure. The slanted price structure, including the restricted convertibility and the adaptation of the reference price system, is the single most important factor which has shaped the Turkish industry.

Despite these measures to keep costs artificially low, the aggregated prices of Turkish drugs grew over the past nine years by 75%. Healthcare costs also increased due to the larger number of patients reaching medical services. Regardless of these incremental costs, healthcare spending has been on a downward spiral since its peak in 2009. After the global financial crisis of 2008 ravaged the Turkish economy, the authorities implemented austerity measures to curb healthcare spending, a target which was dully accomplished. According to a study conducted by the Social Security Insurance (SII) staff, Turkey was able to reduce healthcare spending by 0.5% of GDP within that year. Since than, the economy has largely recovered, but healthcare spending never returned to its pre-crisis levels. Today, healthcare spending stands at US$479.7 per capita, one of the lowest among both developed and semi-developed economies.

In this low-margin price environment, Turkey's robust demographic has been fundamental to the survival of the industry. Turkey's 83 million inhabitants make the country the second most populous in Europe . While a large consumer base is inherently favorable to the growth of the health sector, it is its balanced composition that plays most to Turkey's advantage, with an age breakdown of 20% pediatric, 10% geriatric and a young median age of just over 30 years old, according to World Population Review's latest statistics. Turkey's population is often described by experts as "young and aging," a contradiction that refers to the growing elderly segment, which rose by 17% over the past five years, against a backdrop of an overall youthful demographic. Attracted by the age spectrum opened by Turkey's population, women's healthcare multinational Exeltis entered the market in 2014 to cater to the needs of women from puberty to menopause, as Hulya Yalin, newly appointed general manager, explained: "With its young and aging population, Turkey is an important geography for healthcare providers, allowing companies like ours to find a market across all age groups and stay a partner to women patients throughout their lifetime."

The demographic indicators are also beneficial for the economy. With only 6% of the population over the age of 64, Turkey is left with a strong labor force, of which 38,000 people work in the pharmaceuticals industry. Cem Öztürk, country manager for multinational Sanofi, explained why Turkey is the third largest industrial production site for the drug giant: "Sanofi recognized Turkey to be a lucrative emerging market first from a demographic perspective, given the young population and its knowledgeable and dedicated workforce and secondly because of the country's almost perfect placement between Europe and Asia." ■

INDUSTRY VIEWS ON PRICE CONTROL

"In the current context, a drug sold for 10 euros will be valued at 2.97 euros as a reimbursed product in Turkey, based on the official exchange rates and the National Health Count System Discounts. This system puts immense pressures on the industry, whose ability to innovate and make investments is curtailed."

- İsmail Yormaz, General Manager, Recordati İlaç

"The policies set in place by the Turkish government have brought visible results in the progress of the healthcare system in Turkey, such as the decrease in the mortality rates in the last 10 years; however, Turkey remains an emerging pharma market in terms of the structure of operations and access to health."

- Cem Öztürk, Country Manager, Sanofi İlaç

"The social security system is much aligned to the elections. The government takes power from the medical infrastructure, as happens in other countries. The reference price system, established in 2004, created a strong healthcare base with big advantages to the market."

- Murat Akturk, General Manager, Sanovel

"The biggest obstacle for biomedicines reimbursements is the pricing system in Turkey: the exchange rate is extremely low compared to the normal market. If we calculate the economic contribution of pharma sales, these are found to be unprofitable."

- Serkan Barış, Country Manager, AstraZeneca İlaç

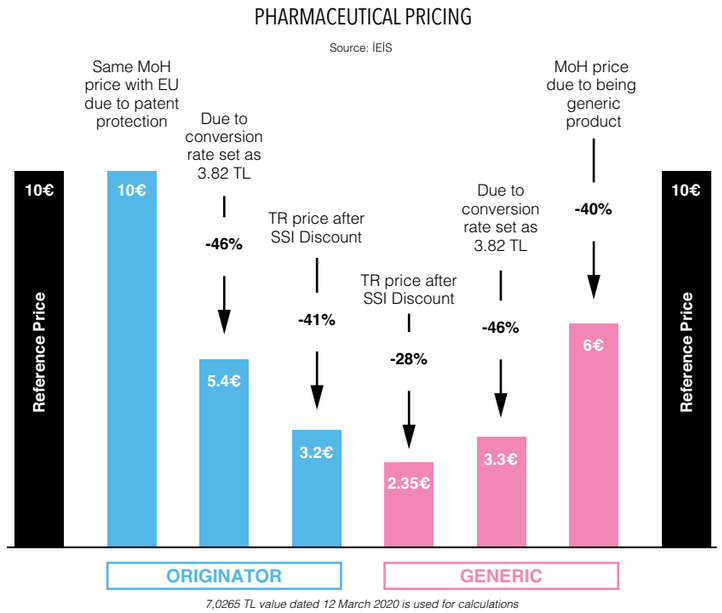
"The Turkish pharmaceutical industry has valuable knowledge, good R&D and manufacturing capabilities and high quality. Our problem is with the price and profitability in the market. Last year we deserved a 45% price increase according to the pricing legislation but was able to receive only 23%. This is a big problem because all of our expenses have increased but we did not get a price increase at the same rate due to the revised pricing legislation."

- Ersan Küçük, General Manager, Drogsan İlaçları

"If people are willing to pay 20TL for a pack of cigarettes, we need to also unlock their willingness to pay the same for a pack of antibiotics."

- Mehmet Goker, CEO, TR Pharm

Economic and Political Tumult, 2018



7,0265 TL value dated 12 March 2020 is used for calculations

With the government acting as a primary buyer of pharmaceuticals, the direct role played by the public sector has made the industry ever more susceptible to political and economic volatility. Since the 2000s, sustained reforms and governmental programs have supported strong economic growth, which has transformed the country into an upper-middle income market. The GDP per capita, according to latest figures, stands at US$10,540.62. Turkey's free market economy relies on a diverse business and manufacturing sector, well-regulated financial institutions and, more-often-than-not, solid public finances. Industry, and in particularly the construction sector, agriculture and tourism, have ensured growth so that between 2010 and 2017, Turkey's GDP growth averaged 7% per year, a stark contrast to Europe's much flatter rate. With Purchasing Power Standards (PPS) growing at 4.9% and per-capita incomes approaching EU numbers, Turkey's various economic indicators were catching up with advanced economies.

Then the 2016 military coup and the subsequent financial crisis and political and economic instability that followed rocked the foundations of Turkey's economic boom. In 2018, the economy reached a cliff as loose financial conditions led to a currency crisis, giving way to mounting debt in the private sector and a growing current account deficit. The TL depreciated sharply in 2018, together with a steep fall in credit supply as inflation surged to over 20%.

In the aftermath of the coup attempt, the government declared a State of Emergency, which effectively paused all economic reforms, especially in terms of improving macroeconomic and fiscal frameworks to align to EU standards. President Recep Tayyip Erdoğan consolidated his power by triggering snap elections in 2018, and the country transitioned to a presidential system, centralizing more power with the leader. Emergency measures were also taken on monetary and fiscal issues and, in the wake of the crisis, the Turkish Central Bank (CBRT) raised interest rates to 24% as a reactionary measure to inflation peaking at 25%. A financial instrument called the LLW (late liquidity window) was also triggered in order to enable banks to make use of excess liquidity and inject more money into the economy. Other monetary instruments followed, including restricting the use of derivatives, banning the use of foreign currencies in high value transactions or forcing transfers of foreign currency proceeds into domestic currency. While the re-election of Erdoğan reassured the markets and the re-stabilization policies eventually brought the fiscal landscape into equilibrium, the measures adopted intensified concerns about the credibility of Turkey's governance and macroeconomic stability.

As far as pharmaceutical companies are concerned, 2018 is recalled as a dark year, as decreasing healthcare spending, shrinking investor confidence and the lira devaluation took a toll on the sector. "Last year was a tough one, if not the worst, for Turkey pharmaceuticals, and the ripple effects of the shock continue to be felt today, albeit to a lesser extent," said Şirin Deha, founder and general manager of Era Pharma, an independent CRO.

As the lira fell to historical lows, pharma companies saw themselves choosing between stopping the importation medicines and thus putting the medical sector into jeopardy, or incurring losses. Zeynep Atabay, owner of Atabay İlaç, chose the second option: "When the euro went up, we continued production despite the losses in order to assure hospitals of uninterrupted supply."

But the crisis also worked as a catalyst for the pharma industry, especially in terms of intensifying efforts for boosting pharma exports and increasing self-sufficiency in manufacturing. ■

Süha Taşpolatoğlu

CEO
ABDI İBRAHIM İLAÇ

The first step was to connect with companies around the world who were already operating in biosimilars. Secondly, we invested in production and established the largest biotech drug manufacturing facility in Turkey. The last component, but just as important as the other two, was to invest in people.

A key milestone is the opening of the biggest biotech drug manufacturing facility, AbdiBio. Can you tell us about this facility?
We realized that biologicals currently represent 20% to 30% of the market and will continue to grow their market share in the future. Today, more than 50% of R&D expenditure in multinational companies is focused on biological products. Given this background, Abdi İbrahim, decided to enter the biosimilar drug manufacturing field in order to stay competitive and to grow our business.
We first decided to invest in this sector back in 2010. The first step was to connect with companies around the world who were already operating in biosimilars. Secondly, we invested in production and established the largest biotech drug manufacturing facility in Turkey. The last component, but just as important as the other two, was to invest in people. Currently we have 30 employees in our bio facility. The facility is not yet operational, but we continue to invest in the education and leadership skills of our employees.

When does Abdi İbrahim expect to launch its first biosimilar product?
We defined three key phases for production. The first phase was to conduct a technology transfer with a company which is already operating in the market, with the aim of preparing a fill-and-finish product. The second phase was to sign a licensing agreement to manufacture from cell lines. The third phase is to develop our own biosimilars. We anticipate that we will be ready to produce our first fill-and-finish products by 2021 and we hope to be launching our own biosimilars by 2025. Abdi İbrahim is also in contact with multinational companies, and our bio facility will be used for the toll manufacturing of biological products.

How do you think Turkey's localization policy might shape competition between local players and foreign players?
The localization policy in Turkey was mainly designed for chemical products, but has now flowed over into the biopharmaceutical area. Looking at the MOH's localization criteria, it shows that in the near future, most biologicals will not need to be localized. On the other hand, there are some biopharma companies that are willing to localize their products for the Turkish market, but they are also willing to use Turkey as a hub because of its geographical advantages. Many companies are keenly aware of Turkey's advantages in terms of production, logistics, and clinical studies, and therefore they want to localize their products in the country. Abdi İbrahim, as a 100% local pharmaceutical company, is supporting the country's localization policies, as we believe that this will help to close the trade deficit and bring technologies and expertise to Turkey.

How has the balance between domestic and international markets evolved?
In 2015, only 10% of our overall revenues originated from international markets. Today that figure is approximately 20%.
At the end of this year, we anticipate raising our international sales by another 10% compared to the previous year, to approximately 100 million dollars. Our medium-term goals are to expand our existing markets, enter new markets, and increase our international sales to US$250 million. In this sense, our primary target markets are EU countries and the USA. We consider every option in our ambition to grow in these geographies, including buying a company. As a strategic goal, we aim for half of our revenues to stem from our international business after 2025. While international operations are very important for us to grow further, Turkey will always be Abdi İbrahim's first priority.

How do you believe the Turkish pharmaceutical market will change moving forward?
I believe that Turkey will see some changes in the social security system, which is currently too difficult to uphold in the long term. We also expect changes to occur in introducing OTC legislation. Many products will no longer be reimbursed and out of pocket payments are predicted to rise. Biologicals will shape the future of the pharma industry and I believe companies should be investing now so as not to be left behind. Production capabilities and capacity in Turkey will attract other countries to bring their production here.
As Abdi İbrahim, we trust Turkey's potential, strength and people. We believe that it would be the right decision for foreign companies to invest in Turkey. ■

Dr. Okan Öncel

General Manager
BİLİM İLAÇ

It is true that it has become difficult to find new products in the generics space and investments are poured into biological products, but similarly to the case of antibiotics, the less competition, the more opportunities for market consolidation for the remaining players.

Could you bring us up to date with the latest developments?
According to its strategic planning process and its results, Bilim has decided to change its chronic treatment area preferences and to focus/invest more on selected treatment areas. Diabetes, respiratory disease and ophtalmology are the main chronic treatment areas that we focus on. Besides, Bilim has strong muscles in areas like ENT, pediatrics, dermatology, gynecology in the acute segment. Looking at the market for oral drugs in diabetes, Bilim has a prominent market share. Similarly, we play a dominant role in the respiratory segment too, and we make important investments in these therapeutic areas. Over the last couple of years, the Turkish economy has been facing many hurdles but, despite this environment, we continue to invest because we have faith in the strategic areas we choose. In this regard, we have just finalized our sterile liquid products facility and started production there. In previous years, we have been confronted with difficulties in terms of our product development. We re-engineered the structure of our R&D and re-engineered the structure of our R&D and new product line. In Turkey it takes about three-four years to develop and launch a new product, so our launches are projected for 2020 or 2021.

The localisation policy was introduced in an attempt to reduce imports. How do you think it will play out?
Bilim's revenue stems primarily from producing for the domestic market, secondly from production for exports, and only thirdly from contract manufacturing. The localisation policy opened up new opportunities in contract manufacturing, either by connecting Bilim with new partners, or by helping old partners expand.

Could you walk us through the process of choosing the products you come to the market with?
Being selective is important because resources are not endless. If you divide your resources too broadly, you may never get a dominant position in one market. For now, we continue to invest on our targeted treatment areas and, in the future, we may add some additional areas. In the meantime, we do not neglect the acute segment which is our core business, even though there is high competition and discounts. Nevertheless, due to its diminishing attractiveness, competitors are exiting some areas of the acute markets, creating space for the remains; e.g. 10 years ago, there were about 15 competitors in the antibiotics space, and now there are only four or five.
Also, I should emphasise that many companies are jumping onto biosimilar products, which account for between 15-20% of the market, and invest in manufacturing facilities, but let us not discount the remaining 80% consigned to the chemical drugs. It is true that it has become difficult to find new products in the generics space and investments are poured into biological products, but similarly to the case of antibiotics, the less competition, the more opportunities for market consolidation for the remaining players.

Could you tell us about your export oriented strategy?
Bilim exports to more than 60 countries. With our new manufacturing plant, we may have more options for exporting more to Europe and North America. But we are becoming more selective about the countries we operate in. If a market does not meet a certain threshold, we re-evaluate our commitment, otherwise, we are faced with a huge workload that only pays back in high hidden costs in time; that's not sustainable.

Do you have a final message?
What foreign investors and partners need to understand about Turkey is the high quality and competitiveness of the country's local producers. Beyond that, Turkish business culture enables easy communication and agreement and both individuals and companies are very flexible. Turkish players have a lot of respect for their partners, especially long-term ones, to the extent that they will be willing to suffer some financial losses in order to maintain a partnership. But, more generally, the size and growth of the market here is promising, and a business started here can be taken anywhere in the world. Apart from the mentioned above, Turkey has quite good opportunities in terms of clinical trials, R&D and biosimilar production. Combining these elements, I genuinely believe Turkey offers great opportunities for all global players. ■

Philipp Haas

Chairman & CEO
DEVA HOLDING

APIs are not always readily available and in order for us to be early in the cycle, we must be able to develop our own APIs, which also gives us a cost advantage. We produce our finished product with our own API and also export APIs to foreign markets.

Could you bring us up to date with DEVA's undertakings in recent years?
In addition to continuing our regular investments to upgrade and further expand our production capacity, Deva has developed a new logistics center. We are entering new technologies with a focus on some key areas such as oncology, where we are continuing to bring new generics to the Turkish market. We have developed a focus on ophthalmology as well, where we are very strong and have launched a generic in dry eye treatment in the Turkish market and a new product that promises double the strength and is therefore unique in Turkey- we have witnessed the results and are proud to realize that this product is serving an important patient need. I believe this is where DEVA excels at: We bring innovative niche products that patients do not have easy access to in the Turkish system, thus contributing to improved patient access.

What is DEVA's strategy in creating strength in specific therapies?
Antibiotics constitute approximately 20% of our business with a more equal distribution on other areas that we are developing, such as ophthalmology and oncology. Looking ahead to the future, DEVA is looking also into the biologics area, however, this is a challenging arena that one cannot rush into. Currently, we invest in biotechnology. We established a biotechnology center and started developing joint projects with TÜBİTAK

Why is API production a priority at DEVA and how does it fit within the company's overall goal?
We acquired our API facility in 2011 and started developing APIs for certain products where the APIs could not be sourced. This is a great asset for us in the market today. APIs are not always readily available and in order for us to be early in the cycle, we must be able to develop our own APIs, which also gives us a cost advantage. We produce our finished product with our own API and also export APIs to foreign markets.

What is your take on the future progression of the Turkish pharmaceuticals market?
The Turkish market is challenging from a pricing perspective and it is becoming increasingly competitive. This means we need to have a constant supply of new products that are close to patent expiry. Targeting first generics puts us into an advantageous position and once the local market is flooded, we take our products to export markets.

DEVA operates different models of growth in export markets, from API exports, contract manufacturing, co-development, and branded sales. Would you like to give us an overview of your footprint and strategy in primary markets of interest?
DEVA has approximately 600 approvals in more than 60 countries. Currently, we export to more than 40 countries and we have increased our footprint in Europe and the United States as well as some developing markets. Our strategy is to develop new products for the Turkish market first as it is our home market and then leverage our position in Turkey to bring these products to markets outside of Turkey. We employ different models based on the country of export where we license our products or form partnerships with distributors. Every market is different; for example, we have our own presence in Germany, which is a tender based market, as well as in Switzerland and some other regulated markets.

What is the vision heading DEVA's growth in the next five years?
Our aim is to strengthen our position in the Turkish market first before consolidating our presence in export markets, too, with an emphasis on Europe and the United States.

Do you have a final message for our readership?
DEVA has a proven strong commitment to R&D with our center being the largest in Turkey. We are also committed to the highest quality standards, which is evident from our US FDA and EU GMP approvals. We believe quality and innovation are key to moving forward, not only for the export markets but also for the Turkish market. Our foundational mottos are that Turkish needs always come first, and second would be that we serve all markets with one quality. ■

Muzaffer Bal

General Manager
ALİ RAİF İLAÇ

In 10 years, we will see more regulation in the OTC market, which will create new opportunities if we do things right. We will have a favorable climate to grow from our foundation and our main strategy will be to add products to our portfolio based on our capacity and ability.

How has the market evolved over the last five years and what are some of Ali Raif's recent milestones?
Since 2014, the Turkish pharmaceutical market has been growing despite facing difficulties. Over the last 10 years, the market has tripled in turnover and grown from 1.4 billion units to 2.4 billion units. This growth can be attributed to an ageing population and improved socioeconomic conditions in Turkey as well as inflation and an increase in drug prices.
We began our business by representing multinational companies and producing under their license in Turkey. Today, we represent many companies as a distributor by marketing their products. In the 1990s, we established our own R&D facility and entered into the generics business. Today, our in-house portfolio of products contributes to 70% of our turnover.

What is your strategy to differentiate your products and meet market demand?
We are focused in a few selected fields, namely cardiology, gastroenterology, anti-diabetes and CNS. In 2018, we added a line of OTC medications. The new products coming into the market are no longer blockbuster products that have huge sales, so we are flexible on seeing products and opening a line if we see potential in registering and marketing the product.

What opportunities do you see in the market over the next 10 years?
In 10 years, we will see more regulation in the OTC market, which will create new opportunities if we do things right. We will have a favorable climate to grow from our foundation and our main strategy will be to add products to our portfolio based on our capacity and ability.

Low margins and profitability leave little room for high spending on R&D. However, Ali Raif's R&D center has been approved by the MOH in 2017. Could you elaborate on the focus taken in R&D?
In 2014, we established an R&D department and, in 2017, we became a certified R&D center. We have a well-sized R&D team that is working productively. With low margins, it is difficult to invest in R&D and it is helpful that the Government provides grants to the industry to encourage R&D. We have several new products in the pipeline, and we are chasing drugs going off patent while searching for new formulations and new applications based on recent technology, such as combination products and complex generics that require more innovation. Price and feasibility are a key factor that determines whether or not we will be able to manufacture our pipeline products.
Currently, we are considering expansion to increase our production capacity. We are not a part of the biotechnology wave and we are waiting to see how it pans out before investing in it or finding a licensed partner.

What is your vision for Ali Raif over the next five years?
Our vision is to maintain a work environment where our employees are happy and feel that Ali Raif is a safe place to work. We are examining the prospect of in-licensing by having more global partners or European sources produce for us. We are flexible and open to importing if we find the right product and company that is seeking distribution in Turkey. We are also open to manufacturing and exporting products if companies are willing to transfer their technology to us. Some multinational companies approach us to market their products and, if the product fits with our line, we take on the task.

Do you have a final message for our readership?
The Turkish pharmaceutical industry has a long tradition with Ali Raif being present since 1928. We have tremendous experience with Western multinational companies and we have grown together with our competition. Over the last 100 years, Turkey has learned to manufacture pharmaceuticals and conduct R&D. We have served the local market for many years and now we are seeing our export business grow as well. Our production facilities are recent with new GMP technologies and a team of hard-working people, making Ali Raif a reliable partner. ■

API Dependency: An Issue of Little Redress

The weak lira brought to the surface another issue that affects almost all Turkish pharma players: Turkey's dependency on imported APIs. Denominated in US$, APIs (together with excipients and intermediates) became prohibitively expensive as the TL slid in 2018. Currently, out of around 250 finished dosage forms (FDFs) only five are produced APIs in Turkey. In the past, there were more API manufacturers, but these were pushed out of existence by international competition, especially from China and India. Şirin Deha, general manager of Era Pharma, believes the government should have done more to protect the industry: "Without governmental policies to support the market, producers were forced again and again to reduce prices until producing APIs in Turkey was no longer viable."

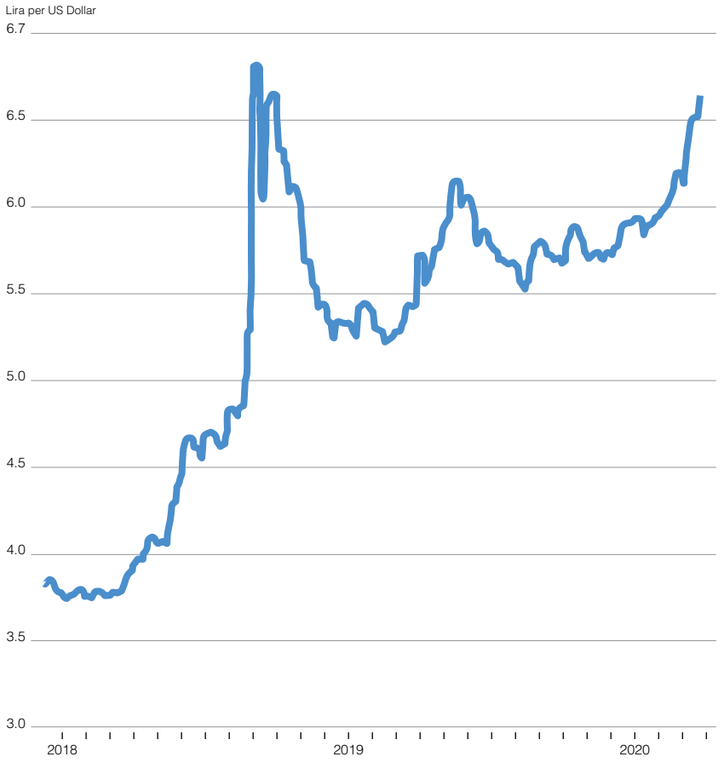
In the market of chemical distributors, Esra Saraçoğlu, general manager of Platin Kimya, is one of the few to express hope for the revival of API production: "India and China began with APIs before integrating forward to the production of FDFs. Turkey could take the reverse pathway, as a developed FDF market that can achieve backwards integration to the ingredient level".

What gives Saraçoğlu hope is Turkey's superior quality. Platin Kimya is negotiating with the government for grants towards the establishment of an API manufacturing plant in Turkey to respond to this gap. Hakan Koçak, CEO of Koçak Farma, one of the few producers of APIs alongside its main formulations business, believes that manufacturing of APIs in Turkey would be challenging because it would necessitate the production of chemicals, which is also an industry that lags behind in Turkey. However, he sees a possibility in Turkey's specialization in niche APIs of high value, which could do well in Europe.

Relying on self-produced APIs gives an incontestable advantage to generics producers as well. Deva Holdings acquired its API plant from Zentiva in 2011, and this self-reliance gave the company control over prices as well as access to the more difficult to access APIs. Besides captive consumption, Deva also sells its APIs, especially in the United States. Atabay is another local company that has put its faith in API production, choosing to pursue backwards integration: "We are working towards enduring brands backed by APIs, to guarantee supply of medicines independent of the state of the global economy and world politics." ■

TURKISH LIRA VOLATILITY

Source: Trading Economics



Esra Saraçoğlu

General Manager
PLATIN KIMYA

Turkish manufacturers, like European manufacturers, face difficulties of competing with China and India in terms of API prices. China and India have superior technology and are a few steps ahead of us because they started the API business before. In these countries, it is only now that they are forward integrating to formulations. Turkey needs more time to first match the quality of APIs globally and then compete against these.

Could you provide a brief introduction to Platin Kimya and how it fits into the larger PLATIN Group?

Platin Kimya is a family-run company established in 1999 with four separate verticals within the parent company: chemistry, agrochemicals, pharmaceuticals and mining. We have 350 employees and a turnover of US$50 million. In 1999, we started an office in Shanghai and in 2001, we also opened our office in Moscow. Our foreign offices oversee the operations of the whole Group, receive our exports from Turkey and receive imports from China, India and Europe. The pharma division of Platin is focused on human health and we started as a chemical business selling APIs and excipients in 2004. We were the sole sellers of excipients with a volume of 4,000 tons per year. We entered the market for finished formulations in 2007, starting business development and in-licensing with one dossier. In 2009, Platin produced our first generic used for oncology and we became the market leader for this product. Today, Platin has 20 dossiers and we are changing our strategy for localization by collaborating with companies to enable technology transfer.

How did the localization policy impact Platin Kimya?

The regulation served as a disadvantage for us at the time, however, we support the Government's decisions. Within the current framework of reimbursements, the MOH (Ministry of Health) is the main player because they are purchasing up to 85% of the total output of our products, and naturally the government would like to protect local production. At that point, we could have quitted the industry, but we decided to stay in the business and appeal to local CMOs of high quality. Even though we do not have a production facility yet, we work with state-of-the-art manufacturers in Turkey. With the Government regulation in place, more manufacturers will increase their quality and begin working towards EU and FDA approval. We have ensured that all our manufacturers obtain EU approval, as our next step will be to export to European markets. Not having our own facility slowed down our growth but, nonetheless, we have managed to register nine products locally, for which technology transfers have been realized to Turkey. We also began exporting to Azerbaijan.

Platin Kimya plays an important role in the local supply of APIs for Turkey. What are some of the trends noticed in terms of Turkey's ingredients supply?

Turkish manufacturers, like European manufacturers, face difficulties of competing with China and India in terms of API prices. China and India have superior technology and are a few steps ahead of us because they started the API business before. In these countries, it is only now that they are forward integrating to formulations. Turkey needs more time to first match the quality of APIs globally and then compete against these.

At this very moment, Platin Kimya is in the process of negotiating for new investment to make a local manufacturing plant for chemicals rather than FDF manufacturing, which is nearing its full capacity in manufacturing in Turkey. Chemicals and intermediates are a point of shortage in Turkey because the imports exceed the exports in this field. We would like to invest in chemicals and pharmaceuticals in the next two to three years for this reason.

What kind of therapies are you positioning yourself in?

Our main therapeutic area is physician and orthopedic medicine. In 2016, we established the first generic with Zoledronic Acid and the first generic of Aclasta for osteoporosis. This was a big milestone for our pharmaceutical business. We are not focused on products with patents expiring in the next few years. Rather, we are focusing on niche products outside of the crowded markets. In 2007, our strategy was to focus on oncology and CNS, because oncology was dominated by multinational companies. Our aim is to compete with Turkish generics companies by finding niche and rare disease products and branding them in order to grow the company in a sustainable manner. ■

Murat Barlas

Chairman
LIBA LABORATUARLARI

Opioid dependence is a specialised and small field, and Liba is the only company in Turkey to specialise in this segment. In the future, we would like to grow our portfolio in other dependencies like alcohol. The market is highly regulated because the active substances used in the drugs are control substances themselves.

Liba has had a long evolution since its beginnings in 1945. Could you introduce our audience to the ways in which the company has changed over the years?
Liba was established in 1945 by Lale and Necip Barlas. Lale Barlas was one of the first female pharmacists in Turkey. Initially a manufacturing company, we changed strategy in 1994 to pursue niche therapies as a distributor. Our portfolio started off with ophthalmology, but soon this was no longer a niche. Liba also explored the oncology segment through an Austrian partner, as well as psychology with a Danish partner, eventually exiting these segments. Today, we continue our line in ophthalmology and we have a focus on neurology, particularly in the treatment of epilepsy, as well as in specialised fields like opioid dependent therapies. Moving forward, we are developing products in the CNS sector. With a turnover of around 40 million euros a year, we are a steady medium-sized company.

Could you explain to our audience what opportunities exist in Turkey for the therapeutic sectors Liba specialises in?
Ophthalmology used to be a fast-paced segment in which new developments kept pharma companies on their toes in expectancy, but this segment has reached a saturation point today. The new generation of ophthalmological products are made through recombinant technology, which is a space we cannot enter into. Liba is not a company that can break into a competitive market with a high volume of original products. On the other hand, opioid dependence is a specialised and small field, and Liba is the only company in Turkey to specialise in this segment. In the future, we would like to grow our portfolio in other dependencies like alcohol. The market is highly regulated because the active substances used in the drugs are control substances themselves. We have to record everything from importation, production and distribution. Our strength is in our niche focus. For this reason, new trends such as the newly popular biotech business brings no opportunities to us.

With new incentives from the government, many classic pharma players are inclining towards the biotech field. As Board Member at IEIS and also the President of the Turkish Biopharmaceuticals Platform (TBP), how do you believe Turkey could better facilitate the growth of the biotech sector?
Turkey needs to develop a regulatory framework of its own rather than simply imitating the FDA and EMA. The upcoming projects in biosimilars and biobetters are very interesting and offer huge opportunities for investments. But the challenge for companies exploring the biotech space is the time these take to get to the market. Technological advancements are helping to reduce time-to-market and thus equipment for establishing biosimilarity should be used in assessment, with the government's acceptance. Besides that, the government has to incentivise biobetters through tenders and reimbursement systems. New incentive systems should be mutually agreed and implemented.

What are your priorities at Liba in the next five years?
Liba's forthcoming growth is predilected on new products in CNS and targeting first generics for products with a real demand in the world and which attract little competition from other companies. In our ophthalmology portfolio, we are differentiating through novel delivery systems - if the development we are working on is successful, it could prove a unique formulation in ophthalmology all over the world. We hope to produce this drug without any preservations, which has not previously been achieved. We also would like to reduce the active substances used in our products to limit side effects. To uphold a strong innovative edge, we outsource our R&D work because our production and labs were closed down.

Do you have a final message for our international readership?
I am very proud of the Turkish pharmaceutical industry and the level of quality it has achieved despite the number of challenges faced in terms of finances and pricing. But there is untapped potential in the country's capacity. In this regard, exports need to be improved with the government's assistance. The quality of Turkish pharmaceuticals should be communicated globally. I hope this can be done in the next few years. ■

Ersan Küçük

General Manager
DROGSAN İLAÇLARI

The Turkish pharmaceutical market is facing pricing problems that will not be solved in the foreseeable future, therefore it is vital to focus on export markets as well.

Could you highlight Drogsan's recent milestones and the company's priorities in the last five years?
Drogsan was founded in 1975 for manufacturing of herbal based pharmaceutical raw materials and over the years, it has transformed into a full-fledged pharmaceutical company serving in numerous therapeutic areas. In the last five years our priority was to focus on niche areas such as, but not limited to, dermatology, nephrology and neurology. Our main objective in both our R&D studies and strategic partnerships has been to bring innovative new products to these niche areas in order to address the unmet needs of patients, while continuing our work in the mainstream market with generic products for general practice.

How do you balance your business between the domestic and international market?
The export markets represented 16% of our turnover in 2019. We are currently exporting our products to nearly 30 countries in CIS, South Europe, Middle East, Central Asia, Southeast Asia and Africa. We are trying to enter new export markets and add products to our existing chain of distribution. The Turkish pharmaceutical market is facing pricing problems that will not be solved in the foreseeable future, therefore it is vital to focus on export markets as well.

How will Drogsan use its R&D expertise to differentiate itself from its competitors in Turkey?
The features that differentiate our R&D from others are a team comprising of valuable scientists capable of multi-faceted thinking and a working environment in which all creative ideas are supported and where multi-disciplinary interaction is encouraged. Our R&D team follows products that are close to patent expiry and attempts to produce the first generics to hit the market. Also we collect new product ideas coming from several departments to develop value added products such as super-generics, innovative new dosage forms, and new drug delivery systems.

What will be your main priorities for Drogsan moving forward?
Moving forward, our focus is on increasing our profit, which currently stands at 15% of our turnover. Over the next five years, we aim to move towards a 20% profit margin so that we can reinvest our profits into R&D and manufacturing for building new products. Without growth, we cannot build a strong foundation for Drogsan and achieve stability.
In the meantime, we see that the biosimilar market is increasing both in Turkey and the rest of the world. However, the biosimilar market will be very crowded in the future because all big companies are investing in this area. We have one product in this field and our strategy in the future will depend on the in-licensing opportunities we find, because our R&D has not been structured for these types of products. Our current biosimilar, which has become the market leader, is also an in-licensed product whose fill-and-finish is done in Turkey, and we are aiming to expand this strategic partnership by product line extensions in the coming years.

What does the industry need in order for Turkey to become a global player in the pharmaceutical industry?
The Turkish pharmaceutical industry has valuable knowledge, good R&D and manufacturing capabilities, and high quality. Our problem is with the prices and profitability in the market. Last year, we deserved a 45% price increase according to the pricing legislation but were able to receive only 23%. This is a big problem because all of our expenses have increased but we did not get a price increase at the same rate due to the revised pricing legislation. The pharmaceutical industry needs to enjoy good profitability in order to invest in the future in biosimilars, gene therapy, and etc. We tried to convince the authorities that the pharmaceutical industry is important for the Turkish economy. If they provide pricing relief, we have huge potential for exports because of the proximity we enjoy with Europe and the Middle East. We need to attract the big pharmaceutical companies to form bases in Turkey. This is a critical issue that will require attention in order for the Turkish pharmaceutical market to enjoy a boom. ■

Serkan Barış

Country Manager
ASTRAZENECA İLAÇ

How does AstraZeneca Turkey fit within the broader umbrella of the corporation, and what are some of its core operations in the country?
AstraZeneca (AZ) Turkey is an important market within AZ Global, International Region and AZ Middle East and Africa both in terms of our commercial and "great-place-to-work" strategies. In Turkey, our main therapy areas are in line with the global business, and we operate in cardiovascular, renal and metabolism (CVRM), respiratory and oncology.
AZ Turkey launched its Serotonin project at the end of 2015 to contribute to its continuous efforts of becoming a "great-place-to-work" by increasing employee engagement. The Serotonin team develop creative ideas to engage with employees based on internal pulse survey results, which are communicated twice a year.

What are the main pillars of growth for Turkey itself?
As of Q3 2019, our main growth platforms are new CVRM, respiratory and new oncology products, but we are generating continuous growth with our mature brands, too.

What are your expectations of how the Turkish pharma and biopharma industry may develop in future years?
Funds allocated for biotechnological medicines are expected to increase as a share of expenses from 20% to 30-35%. The balancing of healthcare costs will be supported by private complementary insurance. Meanwhile, the localisation policy will translate into increased employment and support for innovative medicines. Innovative molecules should be included as alternative reimbursement models are established. However, over-investing in biotechnological facilities may stall the market in the future.

What do you believe to be the biggest challenge confronting Turkish bio-pharmaceuticals?

The biggest obstacle to getting the biomedicines in reimbursement system is the pricing system in Turkey. For the moment, the exchange rate of Euro in Turkey is 3.40, which is extremely low relative to the market.

AstraZeneca is investing up to 5% of its revenues in R&D, and has a rich pipeline posted for new launches in mid-2020 and 2021. Could you elaborate on the need for investment in new medicines worldwide, with reference to one of the new drugs pending?
The pharmaceutical industry is powered by science, research and development. The pharmaceutical sector's investment in R&D is growing and is now more than 165 billion Euros globally. However, we cannot say that there is sufficient investment in clinical research unless we are at the level to solve the problems of all patients worldwide. We should continue to invest in scientific studies especially for clinical research. There are new compounds currently under investigation.

"Open innovation" refers to a model of collaborative partnerships. How could such models be advanced in Turkey to foster breakthrough research?
We collectively stand a much better chance of delivering effective treatments for serious diseases when there is collaboration with pharmaceutical companies worldwide at all stages of drug discovery, biotechs and academic institutions – such as our collaboration with Koç University. With this scientific collaboration, we aim to conduct pre-clinical studies for treatment of diabetes, cancer (such as prostate cancer) and cardiovascular diseases. We made significant investment for pre-clinical researches and we have started our research about the effects of AstraZeneca drug molecules designed for cancer treatment for brain tumour and some stem cell models developed by Koç University scientists. Also, studies related to the carcinogenesis and the binding of AZ drugs to the KRAS receptor which has a drug target, were also carried out. This collaboration will help us discover and develop new drugs.
Our Open Innovation platform provides an open, collaborative approach to link our expertise, unique research tools, optimised molecules, technologies and challenges with your research capabilities and interests. For example information is shared with AstraZeneca UK R&D.
In Turkey, we will expand our collaborations with other stakeholders, research companies through first class research and innovation, building capacity, saving lives and promoting stability and growth. ■

Dr. Ayça Sezer

MD Corporate Business
Development Director
SANTA FARMA İLAÇ

What are the current developments at the company?
We renewed our EU GMP in September with the aim of keeping our doors open for new avenues. In 2015, Santa Farma moved its manufacturing site to a leading-edge manufacturing facility in Dilovasi. The facility is purpose-built and very modern, with a capacity of 150 million packs in one shift, which makes Santa Farma one of the most productive manufacturers in Turkey. We are capable of manufacturing solids, semi-solids, liquids, including specialized forms such as effervescent tablets, sachets, bi-layer tablets and sprays.
Santa Farma has a strong R&D team of 60+ scientists who are developing unique products like value-added generics in different combinations and with new delivery forms.

Turkey is a small market, but it is growing to be competitive. How would you say competition within the generics market has evolved over the years and how does Santa Farma plan to stay ahead of its competition?
The generic industry is very competitive all over the world. Quality is the key aspect through which we can differentiate ourselves. Upon the opening of our new manufacturing site in 2015, Santa Farma obtained its first EU GMP, which was a clear certification for our high quality. Our company culture is that we serve the people and not just the health industry; therefore, we do not tolerate anything less than the very best.
Another aspect which helps Santa Farma to beat its competition is through our manufacturing capacity. With the localization efforts made in the industry, international companies are shifting their manufacturing sites to Turkey. Santa Farma would like to position itself as a production hub within this process.

How would you say the localization policy has impacted the relationship between local and international companies?
Today Santa Farma is cooperating with many international as well as local companies. Currently, we are collaborating with 12 companies four of which are internationals.

How has the product portfolio developed?
We are concentrated on neuropsychiatry, gastroenterology, dermatology, hematology and cardiology. In the future, we plan to include antidiabetics as well.

In previous years, 20% of Santa Farma's total sales were exports. Has this figure changed?
Last year, our exports increased by 52% and we hope to maintain this growth every year. With the market submissions already in place, and market authorizations underway, our exports business is in a stable position to grow.

Besides having a high production capability, Santa Farma also focuses on sustainability and its environmental footprint. Could you tell us more about the measures taken in this scope?
We are a proud member of the United Nations Global Compact (UNGC) since 2010 and we communicate our performance in relation to the 10 principles of the Global Compact on an annual basis. Our yearly report provides information about the progress on Human Rights, Labour, Environment, and Anti-Corruption in line with the requirements of the UNGC. This report has been prepared based on G3 Sustainability Reporting Principles of the Global Reporting Initiative with a view to communicating the corporate performance transparently in line with the principles of accountability in addition to facilitating potential comparisons with the future communications on progress. Looking after the environment is really important to us. We started a zero waste project in our offices by replacing garbage cans with recycling bins. Our manufacturing site has also adjusted its processes to reduce its environmental impact. Santa Farma is a very special company when it comes to valuing people, life and the environment. We have a responsibility towards the environment and the community. We donate blood and stem cells with the organization of Turkish Red Crescent for ten years.

What is your final message for our international audience?
Santa Farma is celebrating its 75th anniversary this year. The average growth rate for the therapeutic groups that we are present is 30%, but our growth rate is at 42%, and we have sustained a higher-than-the-market growth for the last five years. Our vision for exports is to be a top three player in the Turkish market by 2024. ■

EXPORT MARKETS

» Exports are a popular issue in Turkey, not only in pharmaceuticals but across industries. In Dem Ilac' future growth, exports play the biggest role. In every step of our strategy, we created very well-developed dossiers, following the most reputable guidelines worldwide. «

- Deniz Demir,
Chairman,
Dem İlaç

Image courtesy of Recordati

Export Markets

A TALE OF TWO CONTINENTS

A change in direction: Pursuing exports-led growth

Given Turkey's large population, Turkish drug manufacturers have traditionally focused on the Turkish market alone, however, a globalization discourse is starting to take shape amongst pharmaceutical leaders who look to different markets as an answer to the challenging conditions at home: "The Turkish pharma market is facing pricing problems that will not be solved in the foreseeable future, therefore it is vital to focus on export markets as well," said Ersan Küçük, general manager of Drogsan.

Deva, one of the largest generics manufacturers, with over 600 products, has recently incorporated an exports strategy, too: "Our foundational mottos are that Turkish needs always come first, and the second is that we serve all markets with one quality," said Philipp Haas, chairman and CEO of Deva Holding. Operating in 40 countries, the company is one of the few to have penetrated the U.S. market by successfully incorporating its affiliate, Devatis.

Last year, exports were also accelerated by the depreciation of the lira, as medicine prices suddenly dropped, boosting their adherence in world markets. Hulya Yalin, Turkey's general manager for multinational Exeltis, explained how this low-currency environment played out on the flip side: "25% of our sales come from exports, which gave us strength when the lira depreciated last year. While we lost on imports, we gained with exports. We constantly work to find the balance between imports and exports in order to reduce our currency dependency and to continue being able to deliver drugs to patients without interruption."

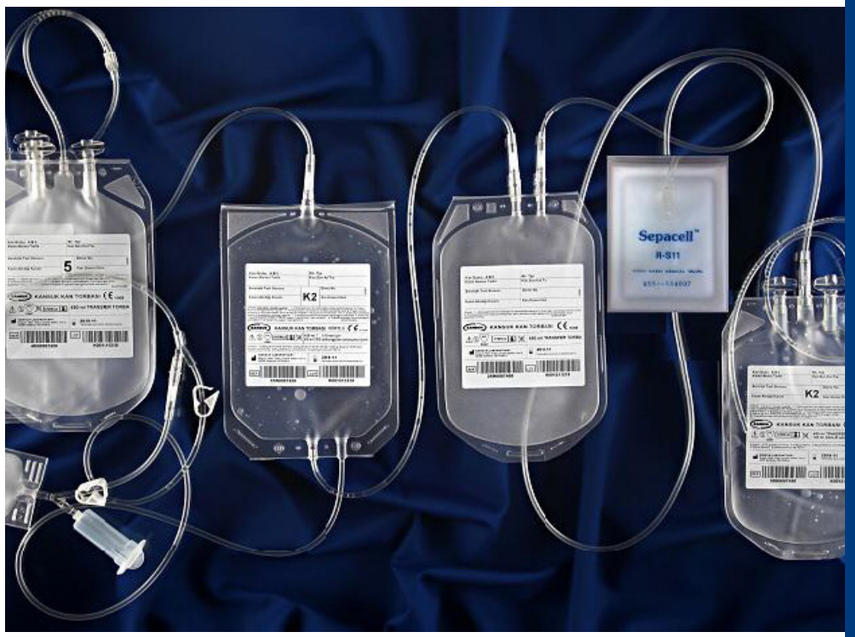


Image courtesy of Kansuk

Turkey's plan to create an economy worth US$2 trillion includes hopes that US$500 billion of this value will be achieved through exports. According to the latest statistics, Turkey's pharma exports reached US$1.4 billion in value in 2019. However, closer examination of this number reveals that while export volumes have grown, the value of exported pharmaceuticals has in fact decreased over the past decade, with the value per kilogram between 2010 and 2018 dropping by 35.9% due to lowered prices concurrent with the currency depreciation. In apprehension of this trend, Turkey's export strategy must encompass high-value products, namely biopharmaceuticals. Cinnagen İlaç is an ambitious biopharma company waiting to receive marketing authorization to start the local production for its 12 products. Once this is received, the "globalization" of the company will commence: "My ambition is to create the biggest Turkish brand in biotechnology by competing worldwide on both quality and productivity," said Ferhat Farsi, co-founder and CEO of Cinnagen. Governmental incentives for exports are also indirectly targeting higher-value goods, which are also the most import-dependent. Funding under the "Strategic Investment Incentive Scheme" is available for manufacturers of products that qualify as import-dependent. The scheme offers 90% tax reduction, as well as a contribution to the total investment of up to 50%. ■

INDUSTRY VIEWS ON EXPORT MARKETS

"The affordability of Turkish drugs is very attractive to neighbouring countries who struggle with their own economic challenges. The Turkish pharma industry has rightfully earned the designation of a producer of both high quality and affordable drugs."

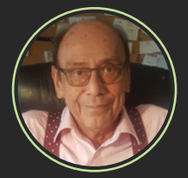
- İsmail Yormaz, General Manager, Recordati İlaç

"Today, the domestic market represents 60% of our business, and exports 40%. Within three years, we expect these proportions to be inversed, and to have a greater foothold in export markets."

- Faik Somer, CEO, Birgi Mefar İlaç

"In the past five years, we changed strategy to export markets, levying our strong position at home in order to expand. We have been exporting to neighbouring markets such as Turmekistan, Azerbaijan and Kazakhstan, as well as other CIS countries."

- Murat Akturk, General Manager, Sanovel



"I am very proud of the Turkish pharmaceutical industry and the level of quality it has achieved despite the number of challenges faced in terms of finances and pricing. But there is untapped potential in the country's capacity. In this regard, exports need to be improved with the government's assistance. The quality of Turkish pharmaceuticals should be communicated globally."

- Murat Barlas, Chairman, Liba Laboratuarları

"Requests for exports are increasing, and we are currently preparing reports for 30 countries for which we have built specific country knowledge; we have three focal international points- in the UK, Croatia, and Kazakhstan, and we aim to increase our footprint in developing markets where we compete with low prices and great industry knowledge."

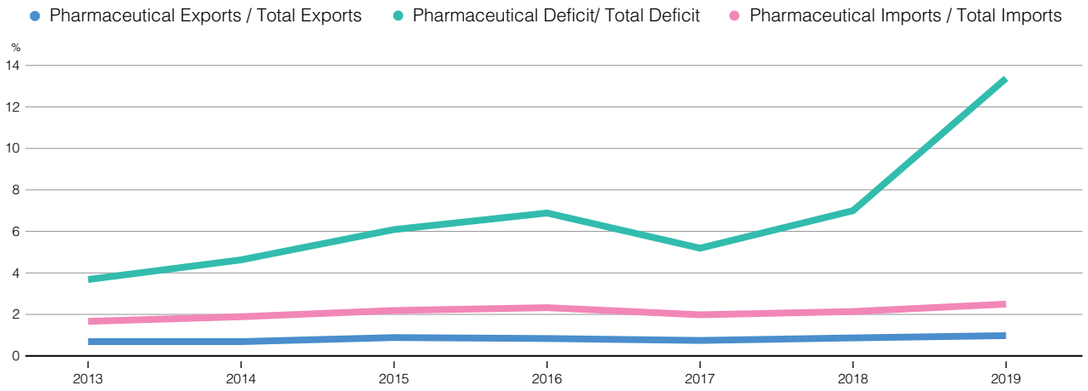
- Dr. Seyfullah Dağıstanlı, Founder, DeltaPV

"The export markets represented 16% of our turnover in 2019. With close to 200 product registrations worldwide, we are currently exporting our products to nearly 30 countries in CIS, South Europe, Middle East, Central Asia, Southeast Asia and Africa. We are trying to enter new export markets and add products to our existing chain of distribution."

- Ersan Küçük, General Manager, Drogsan İlaçları

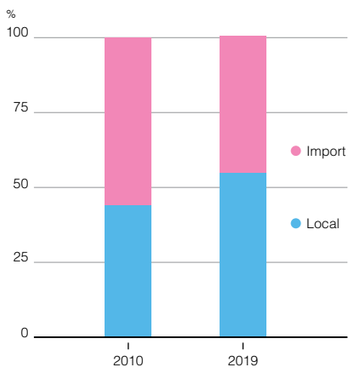
PHARMACEUTICAL PRODUCTS IN TURKISH FOREIGN TRADE

Source: TurkStat, IEIS



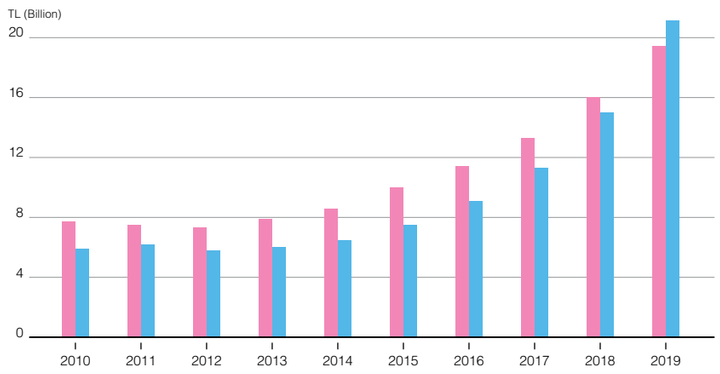
IMPORT - LOCAL PRODUCTS MARKET SHARE (VALUE)

Source: TurkStat, IEIS



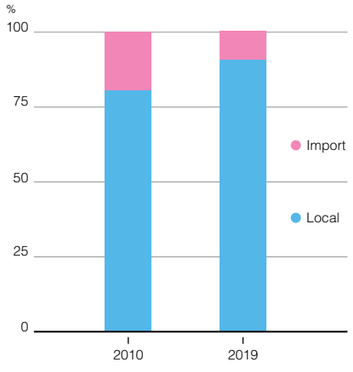
IMPORT - LOCAL PRODUCTS (VALUE)

Source: TurkStat, IEIS



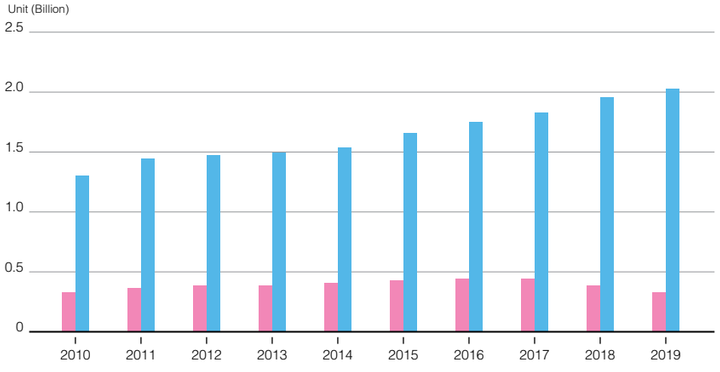
IMPORT - LOCAL PRODUCTS MARKET SHARE (VOLUME)

Source: TurkStat, İEIS



IMPORT - LOCAL PRODUCTS (VOLUME)

Source: TurkStat, İEIS



Defining its Vantage Points: Turkish Drugs in Selected Markets

EXPORTS BY COUNTRY (USD MILLION)

Source: TurkStat, IEIS

	2018	2019	Change (%)
South Korea	354	397	12,1%
Georgia	52	76	47,9%
Iraq	60	73	23,4%
Kazakhstan	40	51	26,0%
Azerbaijan	38	37	-1,0%
Switzerland	45	37	-18,4%
Turkish Republic of Northern Cyprus	30	36	19,6%
Slovenia	33	32	-4,3%
Iran	27	32	18,0%
Germany	27	30	10,7%

Drugs compete in global markets based on price and quality, and Turkey does well at both. Yet, this double advantage has not translated to the expected success in the export of Turkish medicines. The epithet commonly used to describe Turkey as a "bridge between the East and West" is especially pertinent to pharmaceuticals in this regard. The healthcare policy model pursued by Turkey is exemplary of a developed healthcare market, but the price system simultaneously defines Turkey's industry as "pharmerging" – a term used to refer to markets like Brazil, China or India, which have challenged the dominance of Western pharmaceutical hubs through lower prices. With low prices and high quality cancelling each other out, Turkish pharmaceuticals do not fit neatly in either backward or forward Global Value Chains (GVCs).

In its GVC trade with Asia, the MENA region and North Africa, Turkey fares well through backward participation with low value added products and low technology content. Thanks to the rigid pricing conditions implemented in Turkey, Turkish drugs are cost competitive in neighboring countries, too. However, foreign competitors like India come to these low-value markets with a counter offer of even lower prices, which are difficult to match in Turkey. The other half of Turkey's trade in GVC is with Europe through both backward and forward participation. In European markets, prices alone are not sufficient: "European companies are becoming more competitive in price wars because they can invest freely in automation to build bigger capacities; by contrast, Turkish manufacturers are reluctant to invest," explained Tolga Sözen, general manager of Kansuk.

Although Turkish pharma exports reach a total of 169 countries, almost half of the trade value comes from neighboring countries. Nevertheless, Turkish players are gradually shifting their focus from the traditional go-to markets of MENA and CIS countries to the developed markets of Europe and the United States. After 35 years of solely serving the Turkish market, Sanovel, a top ten pharma producer with a product basket produced 100% in-house and that is adamantly opposed to in-licensing products, opened its portfolio to exports only five years ago with an eye on the U.S. market: "Exports are very important, but that does not mean we are engaging our entire portfolio to too many countries around the world; instead, we select in a precise way, and the future promises most from the U.S. market", said Murat Akturk, general manager of Sanovel.

Outside of regulated markets, pharmaceutical leaders are also becoming more selective to reduce risks. Bilim İlaç, which has one of the widest global footprints with 60 countries in the basket, is narrowing its focus to fewer markets: "If a market does not exceed a certain threshold, we will re-evaluate our exports there, otherwise we are faced with huge workloads and many high hidden costs."

These hidden costs reveal themselves to companies around the world: Drogsan's operations in SE Asia and Azerbaijan have been hindered by bureaucratic and economic issues; Santa Farma felt the challenges of political instability in Latin America; Dem İlaç also shared how distributing in countries like Libya requires constant monitoring of daily developments.

In challenging markets, working directly with distributors is less effective, so the best option has been to find the right partnership. Sanovel partnered with Abbott Laboratories in 2018 to enter Russia, an attractive market by size but one that is not easy to navigate. Partnerships are especially crucial for small companies with global aspirations. Tibo, an acronym for "Trends in Innovative Biotech Organisation," is a start-up founded in 2005 by Professor Tanil Kocagöz, who is known for having developed a fast diagnosis kit for tuberculosis. However, running the kits in global markets has not been possible due to competition from multinationals. "While we produce US$500,000 worth of product a year, global competitors produce US$4 billion equivalent," he said. ■

Unacknowledged Quality

The problems presented by the price-quality paradigm extend into the discussion about export markets as well. Turkey offers the lowest priced medications in Europe while adhering to the same standards of quality. However, Turkey's acceptance is eclipsed by its reputation.
"From a regulatory perspective, Turkey is possibly one of the toughest markets because the country does not have its own regulation system and it mirrors the regulations of the FDA, Europe and other countries," explained Zafer Toksöz, CEO of biotech start-up Arven.
Turkey's GMP regulations came into effect in 1984, harmonizing the market with European standards. The TİTCK (Turkish Medicines and Medical Devices Agency) is the official agency overseeing quality compliance for pharma. Established in 2011, the agency's mandate has evolved from a purely regulatory role to a multi-purpose stakeholder in both increasing access to healthcare and supporting the pharma industry. Having completed the first phase of strategic planning between 2013 and 2017, the regulatory body has entered a second stage expected to run until 2022. During this new mandate, the agency is continuing to align its procedures to their foreign counterparts to improve quality compliance and credibility for the industry.
Turkey has not only emulated strict guidelines, but it has also promoted quality at a grassroots level. For example, Dr. Seyfullah Dağistanli dedicated much of his professional life to improving pharmacovigilance (PV) in Turkey: "In early 2000s, the PV system in Turkey was too big and with many shortcomings because it was simply taking after the European guidelines, but copying a pre-given system is not enough as we needed to create a culture of quality", he explained.
Having worked as the head of department for the MoH in 2000, Seyfullah established both the Pharmacovigilance Association and the private firm, Delta PV, through which he is looking to educate the market and instill an industrial culture that places quality above all else.
Although its quality standards are comparable to the rest of Europe, Turkey's pharma industry does not enjoy the same recognition as its more popular European peers for a variety of reasons. Firstly, export markets are less acquainted with Turkish drugs, which have only started to appear globally relatively recently; the more quality, made-in-Turkey drugs that reach international markets, the stronger the Turkish brand will become. Unlike European companies that have created popular global brands, few Turkish firms have developed a prominent enough name to represent the country's qualities. On the contrary, the negative projection of Turkey on the global stage has tainted the industry, impacting the receptiveness of Turkish drugs. "Making people trust that products can be efficiently developed in Turkey is still a hard task. We need to build brand appetite not only for Florabio, but for Turkey as well," said Cem Erdem, general manager of Florabio, a start-up involved in cell line development.
Acknowledging the need to create brand equity for Turkey and Turkish products, the government is running a program called Turquality, designed to turn local players into global names. Successfully enrolled companies receive subsidies for the costs of launching in new markets. Nobel, accepted in the Turquality program in 2015, is the only pharma business without a foreign trade deficit, and it also boasts one of the fastest growth rates. The program has also been extended to service providers, including Ekol Logistics, a Turkish logistics company the size of a multinational and that employs over 8,000 people.
A development that is hoped to raise Turkey's profile as a pharma hub is the country's joining the PIC (S) on 1st of January, 2018. The PIC- Pharma Inspection Co-Operation Agreement is a non-binding co-operative agreement between the different regulatory authorities in the field of GMP. By becoming part of a league of 50 countries that abide by the same universal standards, Turkey sits on equal footing with others countries from all continents. Created by the European Free Trade Association (EFTA), the ultimate goal of the PIC (S) is to remove non-tariff barriers. The agreement exists today both in the form of a formal treaty between European countries (PIC) and an informal arrangement with non-EU countries without legal status (PIC/S).
It is hoped that this milestone will validate Turkey in the eyes of other markets. However, beyond the symbolism of the new label, limited practical change is expected from this official status, at least in the short term. "Turkey entering the PIC is a valuable achievement, but this is not enough. Turkey must achieve bilateral agreements with the different countries that are members, which would unequivocally boost Turkish exports to double-digit growth," commented Ersin Erfa, general manager at Centurion, a company whose new biotech facility was the first to have been inspected by the TiTCK since Turkey joined the PIC. ■

Dr. Seyfullah Dağıstanlı & Aytek Dağıstanlı

SD: Founder
AD: Business Development Manager
DELTAPV


SD


AD

Can you give an overview of DeltaPV?
S.D: After I started working in the private sector I realized that many local companies lack the knowledge to manage their responsibilities in this field. Small companies may not have the budget to invest in and implement a sound system. It was clear that local companies needed the assistance of experts. As a result, the market for contracted pharmacovigilance service companies emerged.

The pharmacovigilance market is projected to double by 2025 worldwide. How do you think this market will evolve in Turkey and are there any recent pieces of regulation that may impact on the demand side?
S.D: From 2011 to 2014, most of DeltaPV's clients were multinational companies who needed extra reporting, which they outsourced. In 2014, a new regulation, the Pharmacovigilance Directive, was implemented and awareness on the topic increased significantly. Within two-to-three months of the directive being implemented, we saw a significant increase in the demand for our services.
DeltaPV dominates the Turkish market and we have a market share of approximately 90%.

What are the core markets served by DeltaPV and how may these evolve in the future?
S.D: Internationally, we have three active focal points, one in the UK, one in Croatia, and one in Kazakhstan. We aim to grow our footprint in developing countries and markets as we believe that we have a competitive edge due to our affordable prices and great industry knowledge.
A.D: Turkey has an advantage in terms of exports as many countries prefer Turkey for its relatively high quality work and cheap prices. Turkey also has a geographical and cultural advantage as it is located between Europe and Asia. Developing countries are important for all pharmacovigilance service providers, but being located in Turkey, we have the advantage of being able to be more cost competitive, we have a culturally diverse understanding and we have an excellent developed infrastructure. Pharmacovigilance is very important and we have the aim to provide the best services in developing countries where awareness is now increasing. DeltaPV also takes on the responsibility to educate the market and to teach those who do not have the knowledge.

What is the added value that DeltaPV brings to its clients?
A.D: DeltaPV's main advantage is that we commit to understanding our client's business and requirements. We offer the entire pharmacovigilance package to customers, but are also willing to provide only part of the package, according to our customer's needs.
Our greatest asset is the software which enables DeltaPV to conduct literature screenings in any language which reads from left to right. We can scan 370 local journals in a relatively short time. This is a great advantage in ensuring patient safety and DeltaPV is one of the only companies that have this capability. DeltaPV provides services to approximately 174 companies.

What is DeltaPV's vision moving forward?
A.D: DeltaPV aims to create awareness and educate the markets about the importance of pharmacovigilance. We are also working on automating the data that we obtain from our searches so that statistics will be available automatically to signal a drug safety problem immediately.
S.D: Pharmacovigilance is important in understanding drugs' behaviors and to increase the safety of the product. Reporting of adverse reactions allows for continuous monitoring of the medicinal product's benefit/risk ratio. Side effects can also give an idea about a new indication or new possible product. DeltaPV is bringing the science and technology together to offer the highest quality services to our customers at affordable prices. ■

Turkey's Standing on the International Stage

"Many speak about the advantages of Turkey's location as a bridge between civilizations," said Ismail Yormaz, managing director at Recordati. "Without denying this asset," he continued, "Turkey's proximity to Russia, the Middle-East, Europe and Africa also creates tensions that surpass the pharmaceutical discussion, but which nevertheless impact the industry.

As Yormaz points out, Turkey's greatest advantage in advancing trade is its privileged geographic position, which allows access to three continents. However, recent developments in Turkey's foreign policy have eroded the relationships with its main partners. Far from being a passive bystander, Turkey has actively instigated tensions that have hurt its global standing on the world stage. Relationships have also cooled between Turkey and its largest trade partner: the EU. Since 1964, Turkey has been close to the EU, later signing the Customs Union and then formally gaining the status of a candidate country in 1999. Relations were interrupted in 2018 when the EU flagged issues with Turkey's rule of law, the judiciary and the obstruction of fundamental rights as matters of serious concern.

Dialogue between the EU and Turkey remains in place, and Kemal Baheci, foreign trade manager of Meksmar Natural and Health Products, highlighted the importance of this fragile dynamic: "Being a member of the Customs Union clears the way for a close engagement with European markets. More than aligning to European regulations, Turkey is also close to Europe culturally. By these criteria, African and Asian countries are accepting Turkey as European."

However, Ahmet Musul, chairman of Ekol Logistics, which operates in a network of 14 countries offering freight services to pharma companies exporting to Europe, believes trade with the EU is not as efficient as it could be: "Restrictions on vehicles and driver checks in a market with supposedly free movement of goods create disappointing and costly outcomes for the company. Our drivers spend too much time and effort to get a visa to only be allowed to work abroad for six months a year."

The uptake of Turkish medicines on world markets ties in with Turkey's ability to create – and repair – its brand equity. The less-visible, yet equally serious repercussion of Turkey's recent domestic and foreign policies is symbolic: it deteriorates Turkey's image in the world. If Turkey remembers the year of 2018 for the economic crisis, 2019 will stay in the collective memory for the intervention into North-East Syria.

In the wake of Turkey's recent intervention into Syria, Professor Fazilet Vardar Sukan, director of the research centre Sunum, said she finds it difficult to establish long-term partnerships with international companies and academic institutions: "In the last two weeks, I had five cancellations of commitments, and this is not due to the success or failure of this centre, but it does reflect on us. I strongly believe that politics should be kept separate from science and technology, but unfortunately this is not the case."

Questions of image and trust are fundamental to the decision-making process when buyers look at the source for their pharma products. Looking ahead to the future, Turkish pharma companies are largely aiming at an exports-led strategy in which foreign markets are not only peripheral but central for growth. Santa Farma, for instance, saw a 55% growth in exports in the past year, a rate that it hopes to maintain in the following years by entering European markets. Abdi Ibrahim, the largest pharma company in Turkey, aims to double its exports revenues by 2025, which now account for 20% of sales.

Today, the current account deficit has shrunk to a 16 years low, falling to US$2.4 billion in May 2019, from US$57.9 billion the year before, helped by the rise in exports and tourism. "Exports are a popular issue here in Turkey," said Ahmet Kuskonmaz, the associate in charge of exports for Dem İlaç, one of the fastest growing companies in Turkey according to IMS. Increasingly targeting the regulated markets, Kuskonmaz expects exports to become the main driver of growth in the future, while five years ago the company did not have an exports department. This shift illustrates the broader perspective taken by many players in the field. "The Turkish market is no longer our main focus", concluded Kuskonmaz. ■

Ahmet Musul

Chairman
EKOL LOJISTIK

Could you briefly introduce Ekol?

Ekol provides best-in-class international freight, warehousing, domestic distribution, foreign trade, customs, and supply-chain management services, with distribution centers covering more than a million square meters, unit trains that enable intermodal transport with 52 runs per week, and a 6,000-strong vehicle fleet. We opened a new era with our Ekol R&D center, established in 2012 under our Technology Group, as we grow with our innovative solutions. We have operated on our own operational software since the 1990s. We became the first company to be included in the TURQUALITY® program, allowing us to export more.

Ekol serves a range of industries by offering comprehensive services. How significant is the healthcare industry, and especially the pharmaceuticals industry, within the broader focus of Ekol?

We need special regulations and requirements for warehousing and distribution services for the healthcare industry due to its prominence. Ekol has the ability to meet the needs of the pharmaceutical industry as we have done since 2010. We operate on principles of minimizing error and damage. Therefore, we are investing in fully automated solutions for collection and packaging operations. We will move to our box ASRS system in 2021, which will prepare orders automatically allowing us to quadruple our current capacity. We are also preparing to serve e-pharmaceutical warehouses so we will have the ability to serve pharmacies and patients. We already consolidated our healthcare warehousing and distribution operations into our Lotus facility.

The International Pharmaceuticals Tracking System is only one of the distinctive features of the pharmaceutical industry. How does Ekol cater for these special requirements, including quality and safety standards?

The world's first Pharmaceutical Track and Trace System was introduced in Turkey in 2010. We provide 2D QR-code and aggregation services and we inform the ministry for both local manufacturers and imported products. We invested in the software necessary for these processes. Our current daily capacity is one million boxes. These "secondary" processes take place in "clean areas," separate from the warehouses

Ekol operates a model of "green logistics". What does this entail in effect, and how do you believe environmental concerns will shape the logistics sector in coming years?

Achieving sustainable growth is our highest priority. We cooperate with NGOs to raise awareness for our employees through training on reducing carbon footprints. In 2014, we succeeded in becoming Turkey's first and only logistics company to obtain the Green Office Certificate, following an assessment by the WWF. We design our work spaces in an eco-friendly manner and implement improvements in savings of waste management, electricity and paper usage.

With the intermodal transport system that we launched in 2008, we lowered our impact on the environment and saved enough diesel fuel to save 730 soccer fields of forest and to travel around the world 360 times. In a single intermodal trip we save 823 liters of fuel, 2,221 kg of CO2, 5.8 kg of NOX and 0.08 kg of particles by not using the road for 2,429 km. We measure our carbon footprint in accordance with ISO 14064-1 and publish results concurrently and we continue to align our investments with our sustainability strategies.

How does Ekol fare in adopting new technology and how would you comment on the broader impact of this trend?

With the developing technology and Logistics 4.0, we are moving out of traditional logistics services to smart warehouses with flexible designs and lower costs. Logistics 4.0 is a trademark of Ekol, as we are turning data into meaningful information by making objects detectable, performing studies on self-determining technologies through the data gathered from sensors, and conducting pilot projects.

How would you describe Ekol's strategy of entering and consolidating a presence in new markets?

We have recently added Sweden to our service network and we manage our operations there under "Ekol Nordics". With this operation center we will connect Scandinavia with Turkey, the Middle East and other countries. Next, we plan on connecting with all European countries.

What do you identify as being the biggest challenge for the logistics sector in Turkey?

The biggest structural problem is the unfair practices of the European Union where we experience unequal restrictions on vehicles and driver IDs in a market with free movement of goods. Our drivers waste time and effort obtaining visas and are only allowed to work abroad for six months a year. ■

Hasan Ulusoy

Chairman
NOBEL İLAÇ

Nobel distinguishes itself not only as one of the largest indigenous pharma companies, but also the only one which doesn't run a trade deficit. What has secured Nobel's success in export markets?
Nobel's presence in foreign markets dates back to the 1990s and, in the past decade, we have been exporting more than importing, at a time when the Turkish pharma industry incurs an annual current deficit of around US$4 billion. Nobel relies on a team of 1,500 employees in 20 countries other than Turkey, with production in two of these countries. But it hasn't always been plain sailing. We experienced major challenges in every place we started our operations, yet we were perseverant and maintained our commitment. Currently, we are the national leaders in drug exports.

How do you believe Turkey could increase its exports and compete in the global market? Are current initiatives in the right direction?
The most profitable route would be to invest into the development of new molecules, but we are not there yet. Given these circumstances, we need to focus our innovation efforts within the existing molecules. The vision of our industry should not be limited to sub-contracted production.

Reflecting on Nobel's evolution since its foundation in 1964, what do you identify as some of the most significant crossroads in its growth?
Nobel's activities started in 1964, and the company was integrated under Ulkar Holding in 1979. At the turn of the millennium, Nobel moved production to Düzce and opened the first office abroad, in Kazakhstan, which was to become the first GMP certified production site in that country. Since our facilities obtained the EU GMP certificate, we went on a growth ramp, with one of our products, Etol, becoming Turkey's highest turnover pharmaceutical. The latest focus at Nobel is our investment in biotechnological and high utility products. In this sense, Nobel joined the Turquality programme in 2014, before starting orphan drugs which were previously dependent on imports in Turkey.

Nobel is the first company supported by the government in the development of biosimilars in line with the 2023 vision. What is the progress made by the company in this sense?
Nobel was the only file selected out of the 28 applications of 23 pharma companies submitted to the bid for "development and production of biosimilars" led by TÜBITAK (The Scientific and Technological Research Council of Turkey). To me, the sine qua non requirement to exist in the future is to be present in the biotechnology market. Market share of biotechnological products has already reached 20% in our country and I have no doubts it will account for 50% very soon. We are determined to be an important player in this segment.

What significance does the Turquality program have for its members?
The Turquality program was designed with a view to create Turkish brands in the global market. It is a project devised to find a solution to the chronic current account deficit problem of our country, and so far it has been an encouraging initiative for the industry.

Investing 5% of its revenues in R&D, and having started the knowledge sharing platform Nobel Medicus, Nobel has played an important role in driving innovation in Turkey. How do you consider Turkey could increase its innovation agenda?
Nobel indeed spares around 5% of turnover every year for R&D activities, but we would like to allocate more, should the conditions permit- that is, if we were not squeezed under price pressures. Nobel Medicus is a unique, peer-reviewed, impartial and free-of-charge journal in our industry. Alike Medicus, I can come up with numerous suggestions for our country's innovation journey, but they all boil down to the same starting point: creating an innovation climate in which every corner of our country as well as the brains of every person operating in the field could act to create an incubation centre. This should be a priority for our country.

What is the vision for Nobel in the coming years and do you have a final message for our audience?
Our vision is "to provide reliable and accessible products for human health at every corner of the world". We have strived for more than half a century for this goal, and we hope to continue in the same line for yet another 50 years and beyond. ■

Hakan Koçak

CEO
KOÇAK FARMA İLAÇ

What are Koçak Farma's most recent milestones?
Established in 1971, Koçak Farma became a prominent player in the Turkish pharma sector, currently employing 1800 individuals and producing over 700 products: specializing in oncology, gynecology, urology, rheumatology, infectious diseases, endocrinology, chest diseases, cardiology and general health protection.
Our focus on oncology since the 2000s allowed us to supply one in every two products in Turkey today. We received the right to sell in the EU in 2005. We produce in accordance with guidelines of cGMP and the WHO. Our acquisition of Eczacıbaşı-Baxter serum group in 2016 remains the only example of the nationalization of an international company in pharma. We manufactured the first biosimilar enoxoparin sodium in 2012 and of insulin glargine in disposal pen form.

Koçak Farma has a very extended product portfolio, with over 500 products. Could you share your strategy in building this portfolio and what are the therapeutic areas that are emerging as the most profitable in recent years?
Koçak Farma has over 700 products but we are a major supplier of oncology and hospital products in Turkey, in addition to being a major player in biotechnological products with our Enoxaparin Sodium and İnsulin Glargine biosimilars. We focus on value added products to maintain continuous growth and leadership in the market.

In an API-dependent country, Koçak Farma stands out by producing and exporting APIs. What are some of the detractors or challenges of API production in Turkey, and how has Koçak managed to establish a presence in this sector?
The main challenge for API manufacturing in Turkey is the lack of raw materials and intermediate manufacturing. Companies have to import the intermediates which is costly. It is also hard to compete with the cost of labor in countries like China and India. To overcome these challenges we focus on products with small consumption in volume and high added value. Turkey has potential in the API area as the closest supplier to Europe if incentives are provided and regulations are modified.

With a global vision, 11 regional offices, and over 25 export countries, what is Koçak Farma's future strategy for consolidating and expanding its geographical footprint?
Koçak Farma is exporting its products to more than 50 countries in five continents.
Our regional offices cover operations in Turkey to reach doctors and pharmacists to promote our products.
In the future, we plan to extend our coverage of export globally and to enter new markets with direct investment with our own production facilities and sales force.

How does Koçak Farma navigate the challenges in the biotech sector?
We have capability to produce both mammalian and microbial products in our R&D and production facilities which were one of the first to be granted approval by the government. We have around 100 scientists working for product development for monoclonal anticores, insulins vaccines and conventional products in our R&D.

What is the outlook for biotech in Turkey?
Biotechnological products have been gradually strengthening their role and market share in Turkey as well as the world. The biotechnological market amounts to 5.4 billion TL and almost 18% market share in Turkey (2018). The molecules out of patent reveal a great opportunity for biosimilars. Pharmaceutical companies must penetrate the biopharmaceuticals market to ensure survival.

Do you believe there is a knowledge gap in Turkey when it comes to biotech, in particular?
It is very difficult to find people with extensive knowledge and expertise in the biotech area in Turkey, because there are only a few companies who locally manufacture biotech products.
Even though companies are increasingly investing in biotech, most of them do not exceed R&D. The government should incentivize projects in biotechnological product development, firstly by constituting legislation for biosimilars and shortening the registration period. It should also incentivize the manufacturing stage of biosimilars. Universities should focus on training students for biopharmaceutical production. ■

Dr. Özdemir Şengören

General Manager
FARMA-TEK

Could you briefly introduce Farma-Tek and its evolution to date?
Farma-Tek was established in 1991 and up until 2014, it was solely a distributor for pharmaceuticals. The company decided to start local production and built the necessary infrastructure in 2015-2016. Today, we have a hybrid model based on originator agreements with international companies, as well as local manufacturing and R&D for generics. The third element of our business is exportation which will dominate Farma-Tek's expansion strategy in the near future. Farma-Tek's decision to localize was not triggered by the localization policy. What drove us to this decision was the evident candidacy of Turkey as a pharma manufacturing hub. Moreover, pricing pressures made it difficult to sustain growth with original products alone. Therefore, we aimed for a hybrid model through which we can act as a local manufacturer for exports as well as utilize the technology transfer with global companies to build on our own R&D and generics. That has enabled us to launch two generics that are the first of their kind.

What underpins the selection process for the drugs manufactured locally?
The majority of our investment is directed towards dermatology. Our second largest area of focus is CNS products, followed by some originals and generics that are in niche treatment areas such as nephrology, hematology, newborn treatments and virology. We are in the process of strategizing these investments, focusing on selected therapies, and it's important to stress we are not interested in the mass markets. Going forward, our strategy is to build on the next generation generics while defining our own niche therapy areas.

What would you comment on the effectiveness of the localization policy so far?
In a market like Turkey, originals and local products-namely generics- are both required. From an authority and budgetary perspective, almost 95% of the population is reimbursed. Drugs are one of the leading portions of the total healthcare expenditure and reimbursed at a ratio of 80-100%, so the message from the authorities is very clear and it is driven by the budget. In order to create a generic, one needs the original product. In a nutshell, for new drug entries to attract investment from global companies, originals in Turkey should be welcome because it is not easy to survive only with generics.

What is your main focus in R&D and what are your plans for the future?
Our R&D is focused on trying to build our own niche while continuing to support key operational areas such as dermatology and CNS. Farma-Tek has also initiated a CDMO model, allowing companies to outsource their research and development activities to us. Our aim is to expand our local production and R&D efforts with both local and multinational partners.

Could you share your foresights regarding the Turkish market for coming years?
I do not expect a major change in market dynamics in Turkey for authorities, investors or local and multinational companies. In the near future, The Turkish market will not rely on either generics or originals because of the healthcare infrastructure and its socioeconomic role. In the mid to long-term, the push-pull negotiations between local and foreign companies are expected to continue. From a geopolitical perspective, Turkey will be one of the major markets worldwide due to its investment in high quality production, along with the growing infrastructure and experienced manpower. Turkey is bound to become a key market for the East, in the fashion of other emerging pharma markets, but with the contention that it will not be as difficult as Brazil or Russia, nor as easy as India. I would refer to Turkey as a "hub", both cost effective and reliable to bridge between developed and emerging markets. ■

Pricing pressures made it difficult to sustain growth with original products alone. Therefore, we aimed for a hybrid model through which we can act as a local manufacturer for exports as well as utilize the technology transfer with global companies to build on our own R&D and generics.

Mehmet Asri

General Manager
POLIFARMA

Please provide a brief introduction to POLIFARMA's position in the market
POLIFARMA was established in Istanbul in 1986, is a local company that provides B2B services in the field of serum and hospital products. In the serum manufacturing site of POLIFARMA the production is fulfilled using area, equipment and subsystems designed and constructed in accordance with the current GMP standards.
POLIFARMA started production in its new site in 2011. All fully automatic serum (LVP), SVP (Vials, PFS, Ampoules, Lyophilized ampoules and vials) filling and packaging machines, started production in the new manufacturing site with the installation of modern technology equipment, designed in accordance with the EU GMP.

What is the significance of POLIFARMA's CAPD product for both the company and wider stakeholders?
POLIFARMA decided to invest on peritoneal dialysis project at the beginnng of 2017. When we focus on chronic renal failure diseases all over the world, we face with three therapies for patients; transplantation, hemodialysis and peritoneal dialysis (PD). Transplantation is distinguished as the first and best option; however, based on donor deficiency it is not the most common one. Hemodialysis seems the prevalent therapy. On the other hand, we tried to analyze the benefits of PD with the help of international articles and congress. Most of the professors confirm to start renal failure therapy with PD if there is no transplantation option. It took almost 2,5 years to commercialize the PD solutions and medical equipment. Our CAPD machine is unique and with this system we are recording and screening all therapy data, giving us the chance to communication between doctor and patient. Thus we are aiming at a comfortable and sustainable therapy for patients that gives them the opportunity to continue their daily and professional lives.

What is the impact of the localisation policy on contract manufacturing opportunities?
The localisation decision was a great opportunity for companies to prepare themselves for the global arena. By this policy, contractors increased the know-how of high technology manufacturing process, invested in new manufacturing lines of high technology products, updated their manufacturing equipment and increased manufacturing capabilities. Also, by being inspected by global authorities, contractors updated their operational procedures and working systems.

How can Turkey create value added products that are competitive on the global market?
Accreditation of R&D is playing a critical role for growing companies and brings new opportunities.
POLIFARMA has made investment by itself for manufacturing of multichamber polypropylene bags. And with this experience, value added product named as Polinuthree 3 Chamber Parenteral Nutrition Bag was born, as a first generic. With this huge investment and experience, we are capable to develop all nutrition bags and oily emulsions, such as Propofol.
For our 2020 R&D strategy we have focused on first generics with the assistance of Tubitak national funds. We also want to expand our portfolio by focusing on the rare disease medications.

Please discuss the evolution of IV fluids market and opportunities in this sector?
Since early 2000's, POLIFARMA is the most sustainable and major player in IV fluids production and sales. Thanks to competition with multinational companies for more than a decade, we built our state-of-the-art facility with the highest capacity in Turkey equipped with brand new technologies. We also presented Polipropyline technology to the country giving hospitals the benefit of safety especially for oncology drug preperations. Targeting both public and private hospitals with our field force, we covered every territory in the domestic market. Manufacturing high quantities of IV fluids needs good planning, storage, distribution channels and communication with the users at hospitals. We are also exporting our IV fluids to more than 15 countries.

What is the vision for POLIFARMA in the coming years?
POLIFARMA was just a IV fluids manufacurer until 2016, when we invested in our Aseptic line and, right now, we have more than 50 products commercialized as vials, ampoules, lyophilized vials and prefilled syringes. We are the first local manufacturer of three chamber parantaral nutritions; also we developed the first local PD solutions with the unique CAPD machinery.
Our vision is to become a global leader in 2025 in the field of hospital products, as a company that integrates and applies the highest technology and experience. In order to achieve this vision, we closely follow the trends in the health sector in the world and continue to make technological investments. ■

LOCAL MANUFACTURING

» One of the most important issues on the agenda of our industry in recent years has been domestic production. Turkey's localisation efforts have produced many positive outcomes in this scope, with investments in new technologies, increased capacity utilisation and higher employment, while imports were diminished. At IEIS, we wholeheartedly support localisation and technology transfers. «

- Turgut Tokgöz,
Secretary General,
IEIS

Image courtesy of Drogsan

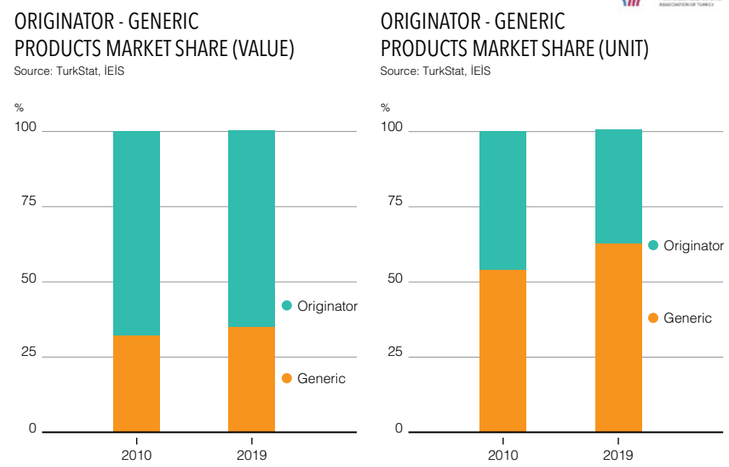
Growing Capacity and Expertise

THE ESTABLISHMENT OF TURKEY'S MANUFACTURING BASE

Turkey's pharmaceutical industry has rich legacies. The foundations of the industry were settled by community pharmacist Abdi Ibrahim in 1912, after whom today's biggest pharma company is named. Between 1928 and 1949, it is estimated there were about 1,500 medicines made in simple laboratories. After the 1950s, the industry began to boom when manufacturing plants proliferated in and around Istanbul, the city that was to become the hub for the nation's pharmaceutical production. With the introduction of GMP guidelines in 1984, together with GLP (Good Laboratory Practices) and GCP (Good Clinical Practices), all manufacturing processes, from registration to patent protection, promotion, packaging, stability studies, bioavailability and bioequivalence, have been aligned to international standards.

At a short distance from Istanbul, Çerkezköy and Gebze are two of the industrial areas where most of the manufacturing sites are based. Çerkezköy is located approximately 100 km away from Istanbul and has good access to the European Highway and Çorlu Airport, both less than 20 km away. The industrial area is the hub of the biggest pharma companies and it continues to attract new investment. Biotech company Cinnagen made an investment amounting to US$100 million in its new manufacturing plant, which is expected to open in 2020. Gebze is another organized industrial zone, home to some of the largest Turkish pharma manufacturers, including Bilim İlaç.

The first drug manufacturing plant in Turkey was opened by Eczacibaşi in the area of Levent, where the contemporary landmark tower of Abdi Ibrahim's corporate offices also resides. Made of fewer than 500 companies, the pharmaceuticals market is highly fragmented, comprised of a few dozen well-established producers and hundreds of satellite players – typically importers coming



to the market in the past decade. Only 81 out of almost 500 pharma companies have their own manufacturing facilities, amongst which 17 are multinationals. The high cost of running a plant is the main deterrent. TR Pharm, a start-up established in 2013, began the construction of its manufacturing plant but had to stop the investment when the expenses exceeded the returns: "Factories are easily financed and built, but running a factory is a cash-burning process that cannot be sustained without operating at high capacity or through product procurement guarantees," said CEO and founder, Mehmet Göker.

According to Murat Çıtıroğlu, founding partner and deputy general manager of Ekin Kimya, only half of Turkey's manufacturing capacity is put to use. Gauging the risks associated with opening a manufacturing plant, most companies are confined to a marketing-only model. The few local manufacturers are also at a loss in the competition with multinationals. Household names like Novartis, Sandoz, Astra Zeneca, Pfizer, GSK, Merck, Abbot, Chiesi, Teva and others have a presence in Turkey; Sanofi alone takes 14% market share of all prescriptions, operating the biggest production site through which it provides manufacturing to another 22 local and multinational pharma companies. However, the dynamics are likely to be affected by two changes: local manufacturers moving towards producing higher-value drugs and the localization policy. ■

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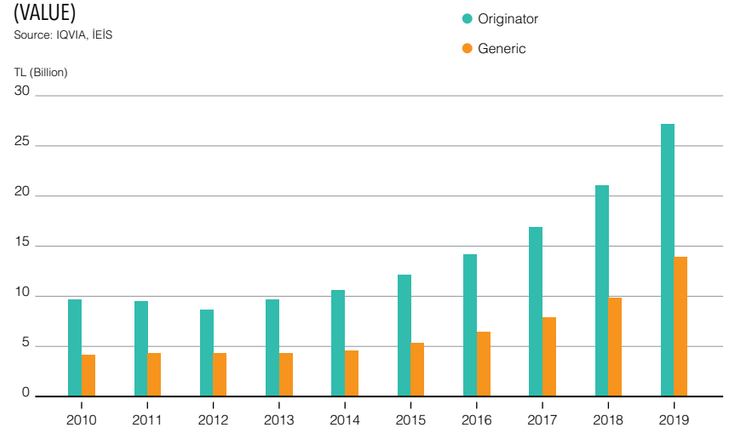
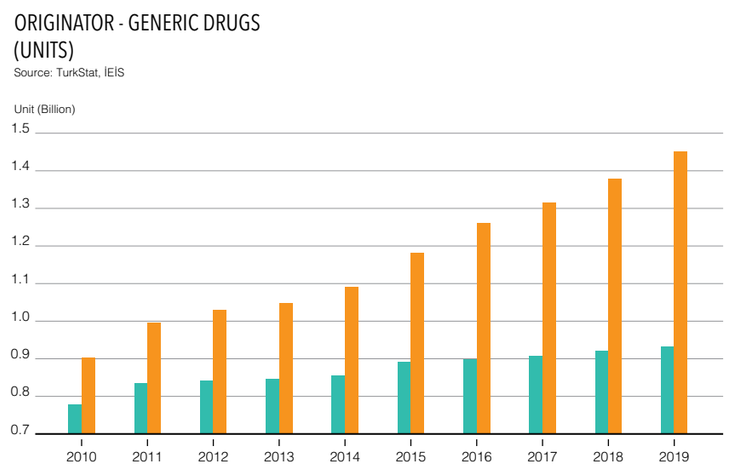




Tolga Sözen & Sibel Sözen

TS: Chairman of the Board
SS: Member of Board
KANSUK LABORATORIES

TS

SS

Could you provide a brief introduction to Kansuk?
Today, our company operates in three key categories: production of medical devices for blood transfusions (blood bags, blood transfusion sets); pharmaceutical products (PVP-I based solutions, suppositories, ors, etc.); and distribution of plasma derivatives.

How does Kansuk participate in export markets?
In 2011, we changed our position by shifting our focus from the domestic market to export markets, particularly to Europe. In Europe, we noticed that prices were too low and that European companies were becoming more competitive in pricing because they can invest freely in automation to build huge capacities. By contrast, in Turkey manufacturers are scared to invest. Even though European competitors can produce cheaper than us through automation, they loose on flexibility as their scale grows. We focused on small, demanding areas and found success. Now we have registered our products in the Nordic countries as well as Spain, Portugal and Italy, and we are trying to enter France and Canada.

What are some of the regulatory challenges in entering foreign markets with products like blood bags?
Regulations for blood bags, more precisely Medical Devices are not as stringent as pharmaceuticals, but it is going more in that direction every year. We have learned the importance of regulatory matters a long time ago based on bad experiences. I now personally spend 30% of my time on quality assurance and solving regulatory issues. Our quality assurance team consists of 10 people and keeps growing. They ensure that we comply with national and international standards, maintain and upgrade our quality management system and technical files for registration accordingly. Regulation is changing in Europe for medical devices, New Medical Device Regulation (MDR) will come into use by May 2020 and be effective in 2024. We have already started to get prepared for this change since 2018.

What in-house training do you offer for your employees and how does that create value for the company?
ISO 9001 was our starting point in 2004, and we felt that these standards benefitted our company. The ISO standard says that management should equip itself with adequate resources for technology and human capital management. We began fulfilling the standards by training our people to increase their qualifications. Many people think that these standards tie your hands, but I believe the better top management understands and applies them, the more benefits accrue. When an audit comes, we take both their observations and nonbinding suggestions and try to apply them.

What is your vision for Kansuk over the next five years?
We have completed our medical devices inspection. However, the pharmaceutical preparations are ongoing and we will apply for GMP approval and a pharmaceutical manufacturing license in the near future. We need to work towards delivering the capacity that we have invested in by designing work shifts on 24/7 bases, meaning three shifts a day for a full week, leading to continuous production. We are investing in quality control equipment according to the latest issues. For medical devices, one doesn't need GMP but we decided to include that too, training our staff, investing in quality control equipment, etc. In our medical devices segment, we have already selected products that we will develop and market in the coming years. In pharmaceuticals, we will concentrate more on exports. We will add new products to our new production lines for powder and suppositories. We also have new products in the pipeline for the distribution of plasma derivatives and will extend our distribution area further. ■

Cem Öztürk

Country Chair
SANOFI İLAÇ

Sanofi hopes to establish Turkey as a market for long-term investment. Turkey has been a reliable market for us and we have invested approximately 1bn USD since we started operations in the country.

How is Sanofi Turkey different from its corporate Sanofi counterparts around the globe?
Turkey is emerging as a market with huge growth opportunities. All five of Sanofi's global business units are present in Turkey. With an investment of 1bn USD, Sanofi Turkey has the largest pharmaceutical production site in Turkey. Our site in Lüleburgaz produces one out of every seven local drugs in Turkish pharmacies, accounting for 14% of Turkish pharmaceutical production. We also provide manufacturing services for 22 national and multinational pharmaceutical companies in Turkey.

What advantages does Turkey have as a manufacturing base for Sanofi?
Sanofi believes in Turkey's potential as an emerging market. The average age in Turkey is 31 years. Turkey has an educated, knowledgeable and dedicated workforce, and the country is also strategically and almost perfectly placed between Europe and Asia. Economic growth has averaged around 6% per year, despite the recent economic crisis. Turkey's pharma market is quite dynamic and its performance over the past couple of years inspires hope for the future. The market is worth 6 billion Euros and grew 26% in 2018 in local currency terms. Continuing strong growth is forecast for the next three years. There is a big transformation going on in the Turkish pharma industry and healthcare system, with a strong focus on drug pricing. At Sanofi we believe it's imperative to reward and prioritize innovation in the Turkish pharma industry in order to realize sustainable growth, a more competitive investment climate and added value for the Turkish economy as a whole.

Does the current localization policy in Turkey influence the dynamics between local and international companies, like Sanofi?
With our 60 years of presence, high localization rate and strong footprint in Turkey, we prioritize projects and cooperation opportunities that will provide value-added to the country. We believe in the importance of prioritizing and rewarding innovations that could improve public health and the country's economy.

What are the future investment priorities for Sanofi Turkey?
We are continuously investing in our operations, both in manufacturing and in R&D. We have invested almost TL300 million in R&D and clinical trials in the last five years. We have also invest heavily on local production capabilities. Out of total production, 86% of our Sanofi products portfolio is produced in Turkey. We continuously assess our current operations against changing market conditions. We have a strong portfolio in cardiology, diabetes, CNS and vaccines. We have a very strong investment project in diabetes, and we are evaluating the rare disease segment.
Sanofi has a strong product pipeline globally with a focus on biological products, investing 6 billion Euros every year in R&D. Currently, we have 81 projects in development, including new molecular entities and additional indications.

How is Sanofi adapting to the price regulation system in Turkey?
Sanofi believes that government policies, such as the reimbursement scheme for example, have brought visible and progressive results over the last 10 years, including a decrease in the mortality rate.

How do you believe the Turkish pharma and biopharma industry will develop in coming years?
Sanofi hopes to establish Turkey as a market for long-term investment. Turkey has been a reliable market for us and we have invested approximately 1bn USD since we started operations in the country. We have achieved considerable success so far in our efforts to grow our presence in Turkey and created added value for the country. We aim to increase our contribution and enhance our presence even further over the next couple of years. ■

Ersin Erfa

General Manager
CENTURION PHARMA

Looking at countries like Korea, Egypt, India or Argentina, one notices that the biotech sectors achieved success because authorities conferred market protections on them. In Turkey, there are more than 13 biotechnology companies, but if we look at market shares, not one of them is in a strong position to grab a higher market share.

Several years ago, Centurion stated ambitions to grow by 150% by investing in specific areas like injectables, orphan drugs and biosimilars. How has this vision evolved?
Today, we are investing heavily in R&D, with more than 5% of our revenues allocated to boosting innovation and development. Recently, we have also received GMP certification for our biologics production, and we are planning investment in vaccines. Reflecting today on the undertakings of the past five years, I can only be happy with the evolution of the company.

Centurion invested into the second largest biotechnology plant in Turkey. What trends underpinned the decision to go forward with this recent investment?
The global biotechnology market takes perhaps more than 20% of the total market share of drugs, and we expect that percentage to double in coming years. Such strong data gave us the impetus to invest in this sector, especially since we were already active in vaccines and plasma products. Currently, we are conducting technology transfer to Turkey in some molecules and, in due course, we will produce antigens too in Turkey. In terms of our therapies of focus, we are mainly targeting chronic diseases, as well as rare diseases, hospital injectables and vaccines.

The new biotech facility was the first inspected by TİTCK since Turkey joined the PIC (Pharma Inspection Co-operation Agreement) in 2018. How do you believe entering into this agreement will help Turkish exports in coming years?
Turkey entering the PIC is a valuable achievement, but we should not forget that this is not enough; Turkey must achieve bilateral agreements with the different countries that are members of this association. At the moment, this is not the case and therefore the next steps would be to sign mutual recognition agreements that would unequivocally boost Turkish exports to double-digit growth.

What gives Centurion the competitive advantage in plasma products over competitors in the 42 countries where is positions this product?
Our strong presence in these countries can be attributed to the unique technology transfer and exclusive distribution agreements that we have secured with our partners in Europe; while our partners are focused on manufacturing, including technology and quality of production, Centurion complements through a strong focus on marketing and sales.

The biotech sector is a very high-risk, capital-intensive market. What prospects do you believe Turkey has in this much-hyped sector?
Looking at countries like Korea, Egypt, India or Argentina, one notices that the biotech sectors achieved success because authorities conferred market protections on them. In Turkey, there are more than 13 biotechnology companies, but if we look at market shares, not one of them is in a strong position to grab a higher market share. The authorities need to step in to protect local industry players. And local producers should focus their technology on molecules or antigens, and not just resign themselves to fill-and-finish projects.

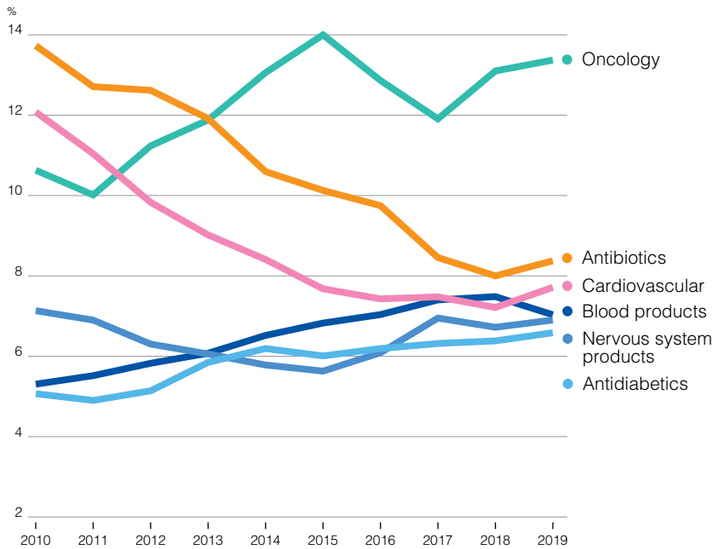
Can you elaborate on the significance of the collaboration with Neovacs to launch the first drug for Lupus?
Phase 2 studies have been successfully finalised and announced. Lupus is a very important rare disease, affecting especially women between the ages of 20 to 40. The treatment for the disease is very costly for the social security budgets of different countries. We expect that Phase 3 studies will be finalized in the next two years and the product will be launched worldwide.

Can you share with us what comes next in terms of priorities laid out by Centurion in the medium term?
The vaccine business is the most crucial component of our business today as we prepare to make localizations for three vaccines, from antigen to fill-and-finish. In this way, we will attain independency, using live and recombinant technology vaccines. At this point, we have already signed the technology transfer agreements, and we find ourselves at the stage of discussing regulation issues with government. ■

Finding a Place in the Right Therapies

Increased competition and low margins have motivated manufacturers to make changes in the repository of their drugs and look at long-term, lifestyle diseases in the chronic segment. The trajectory of Turkish generics manufacturers has diverged from the acute segment to multiple therapies in the chronic segment. Traditionally, generics companies produced antibiotics and other medicines for acute diseases. Even if today antibiotics still account for over 8% of new drugs launched in the past year, many players have either left or reduced their footprint in favor of a more widespread focus in the chronic space where margins are higher. Deva İlaç, one of the largest pharma companies in Turkey, used to have a portfolio dominated by antibiotics, but today antibiotics constitute 20% of the business: “Our strategy was to broaden our perspective in alternative focus areas rather than continuing with an antibiotics dominated portfolio,” explained Philipp Haas, chairman of Deva.
According to Okan Öncel, general manager of Bilim İlaç, 10 years ago there were 15 companies in the antibiotics space, but only five continue today. Bilim maintained its core focus on antibiotics, but not without also taking cautionary action in diversifying its portfolio by expanding the pipeline to diabetes, respiratory and oncology drugs, as well as investing in new sterile liquid products. Redesigning a product portfolio and adapting the production requirements to each type of drug is both time consuming and costly, and it will take Bilim another four to five years to see its new lines on the market.

THERAPEUTIC GROUPS ON VALUE SCALE
Source: IQVIA, IEIS



Rather than spreading their resources thinner across multiple therapies, many companies have taken the opposite approach and invested in a specific sector with high entry barriers. One of the few remaining manufacturers in the antibiotics space, Tüm Ekip, became one of the biggest by investing in a specialized injectables facility: “There are fewer and fewer producers of antibiotics, especially in Europe, but new antibiotic solutions are always necessary as infections become resilient,” said Tüm Ekip’s CEO Ahmet Altuğ Oğuz.

Tüm Ekip is now the world’s third largest manufacturer in injectables, according to CMS Hospital Index (2018). Similarly, Eczacibaşi is a market leader for radiopharmaceuticals; manufacturing this type of medicine is ridden with challenges – from the short life spans of the product, to the safety and regulatory precautions and the high technical expertise required. By tackling these challenges, the company has maintained round-the-clock, decentralized production in five manufacturing sites both in Turkey and in neighboring countries.

In the same fashion as multinationals that are recognized for their dominance in a particular therapy, such as Recordati for rare diseases or Exeltis for women's health, Turkish companies seek to associate their brands with a signature therapy in which they can feature as an authority in the field. Santa Farma follows this philosophy, seeking to become an expert in neuropsychiatry, gastroenterology and dermatology – segments in which it enjoys above-market growth.

Santa Farma is a well-established company having celebrated its 75th anniversary this year, as well as boasting a record production capability as the company capable of manufacturing the highest volume in a single shift. Smaller companies that do not rely on manufacturing have a harder time finding their place in the market, especially because the popular chronic segments like cardiology or CNS are occupied by multinationals while the rest are fought over by local big pharma. Boxed out by the bigger companies, new market entrants are obliged to look for less saturated markets to increase their chances of launching a first generic or a super-generic. Liba, a medium-sized company with a turnover of €40 million a year, had pursued ophthalmology as a niche area, but soon this became more crowded. Today, the company has re-profiled in dependence therapies, a highly regulated market that has discouraged further competition. "Companies that compete in the simple generics market are just rounding the wheel, while new entrants have little hope for survival in the long term," said Deniz Demir, managing director of Dem İlaç, one of the fastest growing pharma companies in Turkey, according to IMS rankings.

Growing at 13% CAGR inflation-free mark, the main contributors to the industry's growth are larger volumes coupled by the launch of new products. However, to launch new products, manufacturing needs to be complemented by an R&D program. Perhaps more than greater facilities and networks, multinationals' biggest asset is their R&D power through which they create generics with a difference. "If we want to claim the 60-70% of the market currently covered by multinationals, then we need innovative products and strong R&D," said Okan Öncel, general manager of Bilim.

R&D has been severely neglected by generics companies when compared to the investments made by their multinational peers. Even large companies like Deva spend no more than 5% of their revenues on R&D. Moreover, the CRO market is underdeveloped, limiting the options for manufacturers without their own R&D lab. Era Pharma is the only independent CRO recognized in the country and this recognition occurred almost by coincidence. The MoH agreed to audit Era only when the existence of an independent CRO was counted as a pre-requisite to Turkey's entry in the PIC (S) earlier in 2018. Previously, there was no definition under GMP regulations for an entity whose sole purpose is R&D. The CRO business model has proven difficult for Era Pharma, especially during the financial crisis of 2018, when government support stalled and clients stopped paying. R&D became the first expendable service. In the future, Era Pharma looks to have its own pilot manufacturing plant: "Without this plant, we are sending our clients to CMOs, when we could ourselves cash in on that revenue," said Şirin Deha, founder of Era Pharma.

Volume manufacturing has been prioritized over the development of innovative products, but the trajectory taken by generics manufacturers indicates that R&D will be gaining more prominence. Turkey currently ranks 59 out of 142 countries in the worldwide Innovation Index, behind other countries with a strong pharmaceuticals industry such as Brazil (31), India (35) or China (47). Although R&D expenditure has increased at 19.1% CAGR between 2010 and 2017, the total expenditure only represents 1% of GDP, which is well below the EU average. By 2023, the government aims to bring R&D expenditure to 3% of GDP. If the industry manages to grow steadily while remaining economical in terms of R&D investment, an influx of public funds in R&D would help to transform the industry's profile from a simple generics market to a specialist, high-tech manufacturing hub. ■

Şirin Deha

Founder & General Manager
ERA PHARMA SOLUTIONS

ERA Pharma Solutions is a contract research organization (CRO), established in 2010 to provide drug discovery, development and lifecycle management services for the pharmaceutical industry.

Could you start by bringing our audience up to date with the latest development at Era Pharma?
Era Pharma is the only accredited independent R&D laboratory for the pharma industry in Turkey. In the latest of our achievements, Era was audited by the MOH as a pre-requisite for Turkey to enter the PIC/S membership, which was realized in 2018.

How is the status of a GMP accredited R&D centre changing the prospects for Era Pharma?
We are the only organisation enjoying this status and it allows us to conduct analysis for different companies which we could not carry out before. Both domestic clients targeting export markets and foreign pharma companies entering Turkey require an independent R&D centre, in turn accredited by the MOH.

Why is Era Pharma still the only independent CRO and other companies haven't emerged with the same model?
Providing high quality service for a long time is a very expensive and laborious task for R&D companies. There are R&D incentives in Turkey but, unfortunately these are inadequate and mainly in tax benefits and none of them are up front. Big branded generic pharma companies in Turkey, like Deva, Bilim, or Abdi İbrahim already have their own R&D, but they still work with us, because we present them a predictable and manageable time & risk share for their R&D projects and practical solutions, which require deep market experience and a high expert level of knowledge. However, our main customers are mid-sized players, who cannot sustain their own R&D. We offer SMEs an opportunity to develop and launch their own, local products in the market, without having to import. However, confidentiality is a core aspect, especially since a project can run for years. I would say the model we have in place at Era faces many challenges across many dimensions, which deters other players from entering this field.

How has the localisation project impacted your business relationships with foreign and local partners?
The localisation policy has helped us obtain more contracts with customers because small or mid-sized companies who used to rely only on imports are now required to produce in Turkey. Without the technical production and R&D facilities, it is very difficult for such companies to transfer the product to Turkey, and thus they need not only CMOs, but also CROs who can execute the dossier transfer for them.

Taking into account factors such as macroeconomic instability, but also incentives to boost R&D, could you paint an image of how demand for R&D outsourcing is being felt by Era?
Last year was a tough one, if not the worst, for Turkish pharmaceuticals, and the ripple effects of the shock continue to be felt today. Government support was stalled. When the macroeconomic environment is in bad shape, outsource services companies are one of the first to feel the tumult. Unfortunately, we are not able to cut costs much, because we need well educated, high quality personnel whose expertise ranks above that of the biggest pharma companies, in order to create a persuasive argument as to why companies should bring their more difficult projects to us. On the other hand, clients can cut costs by outsourcing their projects, but outsourcing R&D is still a new idea for Turkey and many are not exploring this option yet.

What are the plans for Era Pharma in the foreseeable future?
One of our core ambitions is to have our own pilot production plant. Without this plant, we are sending our clients to CMOs, when we could ourselves cash in that revenue. Moreover, if we are to aim for FDA approval for registration dossiers, we would need to produce the first batch in-house, which would be another bottleneck to our business. Secondly, Era is looking at opportunities in the biotech sector, which is an important sector starting to shape up. ■

Pelin Işçener

Marketing and Sales Director
ECZACIBAŞI MONROL NÜKLEER ÜRÜNLER

Could you give our readers a brief introduction of Eczacibaşi Monrol Nuclear Products?
Eczacibaşi Monrol specializes in producing agents for PET (Positron Emission Tomography) and SPECT (Single Photon Emission Computed Tomography) scans, which are critical for detecting cancer, cardiological diseases and brain disorders, among other serious diseases. Being the major player in the conventional PET& SPECT business, Eczacibaşi Monrol is also successfully positioning itself as a key market player in "Theranostics", which is a combination of “diagnostics” and “therapy”.
Eczacibaşi Monrol has started local production of the therapeutic agent called lutetium chloride, a radio-pharmaceutical precursor.

Eczacibaşi Monrol is a pioneer of nuclear medicine in Turkey, having introduced many radiopharmaceuticals to the market. Could you tell us about the advances made in this new field?
Eczacibaşi Monrol introduced conventional radiopharmaceuticals to the Turkish market. Nuclear medicine has always been recognised as a diagnostic field, and now it is proving its value in the therapeutic field too. We expect the growth of nuclear medicines to be boosted by the trend towards diagnostic agents paired with therapeutic agents.
Being the major player in the conventional PET& SPECT business, Eczacibaşi Monrol is also successfully positioning itself as a key market player in this new area, called "Theranostics", which is a combination of 'diagnostics' and 'therapy'.
This is a growing concept where the diagnosis and the relevant therapy are used in parallel in targeting diseases such as prostate cancer and neuro-endocrine tumours.
Eczacibaşi Monrol has started local production of the therapeutic agent lutetium chloride, a radio-pharmaceutical precursor. We are very proud to be the first in Turkey and one of the pioneer companies worldwide to produce this agent.
The "Theranostics" concept requires a multi-disciplinary approach involving nuclear medicine specialists as well as uro-oncologists, urologists, endocrinologists and medical oncologists in the decision of the best therapy for the patient. We are currently working to create awareness of this emerging approach across the related fields of medicine.

What are some of the challenges faced by Eczacibaşi Monrol in the production of radio-pharmaceuticals?
Radio-pharmaceuticals are both similar to and different from conventional pharmaceuticals. One major difference is dealing very short half lived radioactive materials which can’t be maintained with an inventory stock. Related safety regulations are also challenging, such as regulations on safe handling conditions and the need for operational excellence due to the very short life of products. These factors require stringent adherence to a multitude of safety and health guidelines. The volatility of radioactive materials also creates production challenges; some products need to be finalised on-site, at the hospital, which requires special technical expertise.

What is Eczacibaşi Monrol’s vision in terms of international growth?
Eczacibaşi Monrol is already selling its products in the EU, MENA and Far East countries and has EU GMP certification. In addition to exports, Eczacibaşi Monrol owns production facilities in Bulgaria, Romania and Egypt, and operates facilities in Iraq, UAE, Pakistan and Kuwait. With the expertise it has gained from operating numerous facilities in a variety of countries, Eczacibaşi Monrol also provides services to customers around the world on constructing plants, installing equipment, setting up quality systems and operating production facilities.

What is your final message?
Eczacibaşi Monrol believes that the market for nuclear medicine is one of abundant opportunity and will soon be recognized as a “speciality” as more therapeutic solutions are discovered. Nuclear medicine will become a key component of targeted therapy, which is intrinsically dependent on targeted diagnosis.
Eczacibaşi Monrol is committed to providing the most reliable delivery of the best quality and most innovative products, not just within Turkey, but to many parts of the world. Our highly qualified team is completely dedicated to achieving our commitments and our success is driven by the team. Sustainability and innovation are two of our core values, and we strive for continuous improvement in our operations and products while trying to serve patients all around the world. ■

Ahmet Altug Oguz

CEO
TÜM EKIP

Tüm Ekip was established in 2000 and is a specialized injectable pharmaceutical producer, with capability to produce seven different sterile forms.

Could you please introduce Tüm Ekip?
Right after establishment in 2000, Tüm Ekip started to develop generic formulations and to obtain registrations. In 2009, the company opened its first production facility. From there, we expanded our capabilities year on year.
Today, we are the only company specialized in injectable pharmaceuticals in Turkey and the only company which has seven different forms of injectables - powder, liquid, lyophilized powder, SVP, LVP, PVC, and non-PVC bag. We are also the only company in Turkey that has a dedicated sterile carbapenem production facility. With the opening of our dedicated injectable penicillin facility in 2014, we became the first and only Turkish company that has three dedicated and separated Beta lactam production facilities. Tüm Ekip is one of the few companies which can produce sterile lyophilized vials and has recently opened a production facility focused on this space. Approximately 65% of our production is going directly to hospitals. We have over 110 products registered in Turkey as well as 20 in other countries worldwide. As per the IQVIA Hospital Index of 2019, Tüm Ekip is ranked third in Turkey in the injectables space.

In the generic space, there seems to have been a shift away from antibiotics and acute therapies to chronic disease. How has Tüm Ekip responded to this trend?
There are fewer and fewer producers of antibiotics, especially in Europe, which presents a great opportunity for Tüm Ekip. The first products launched after the establishment of the company were penicillins. The types of antibiotics that we produce include penicillins, cephalosporins, carbapenems, systemic antibacterials, systemic antimycotics, aminoglycoside antibacterials and macrolides. New antibiotic solutions are always necessary as infections become resilient.
We are a certified R&D Center by Ministry of Industry and Technology of Turkey. Our R&D Center is strongly focused on developing (with QbD) essentially similar pharmaceutical dosage forms needed in clinics and to present high quality, safe and affordable generic solutions, attaching paramount importance to quality and ensuring such quality during the design process. Our R&D department develops injectable dosage forms in compliance with the guidelines of International Conference on Harmonization (ICH).

What other therapeutic does Tum Ekip cater to?
Tüm Ekip develops and produces antibiotics, agents against amoebiasis and other protozoal diseases, systemic antihistamines, antiemetics, gastrointestinal products, peptic ulcer products, systemic corticosteroids, anti-inflammatories and antirheumatics and diuretics. Our latest product is an anaesthetic used in operations.
Our expertise is in injectables. Up until now we have been focused on conventional injectables, but we want to diversify into the biotechnology space. We have already started to produce heparin, which is a very basic biological product, but a step in the right direction to increase our capabilities within the biologics space.

What are Tüm Ekip’s objectives moving forward?
Tüm Ekip has 110 local products and the aim is to have all these products registered internationally. The next goal will then be to reach 500 registrations worldwide. We already export to 25 countries, but we aim to significantly increase this number moving forward. We are currently in the process of launching some of our products in Europe. Another objective is to establish a production facility outside of Turkey to be able to more easily serve international markets. We will firstly look at expanding our footprint in Europe before further expanding worldwide. We will establish our presence where the investment is lucrative.

Do you have a final message for our international readership?
Turkey has a very strong understanding of pharmaceutical production. We have European standard facilities where we produce the best quality products. We are committed to make pharmaceutical products which are accessible as well as affordable to patients, and this gives Turkey its competitive advantage. ■

Hidden Opportunities in the OTC Market

Given the price pressure on Turkish drugs, the OTC market becomes a valuable proxy point for manufacturers to find price relief. However, current regulation does not define a special OTC category, only referring to non-prescription products, such as non-prescription medicines, medical devices, food supplements, vitamins, etc. Nonetheless, there has been growing anticipation that OTC legislation is finally to be introduced. Süha Taşpolatoğlu, CEO of Abdi Ibrahim, shares this expectation: "We believe changes are bound to occur in introducing OTC legislation; with that, many products will no longer be reimbursed and out of pocket payments are predicted to increase," he said.

As the OTC market is growing worldwide, the government has been under pressure to liberalize the sector by introducing a clear legislative framework. The current legislation makes a distinction between prescription and non-prescription drugs without detaching the second from the legal requirements asked of the former. According to Article 1 and Article 24 of the Law on Pharmaceuticals and Medical Preparations it is stipulated that both prescription drugs and OTC products cannot be commercialized outside of authorized medical or pharmaceutical premises. Furthermore, while in European countries and the United States, OTC demarcated products are defined as a separate entity of drugs freely advertized on different channels, Turkey provides less clear boundaries. Non-prescription medicines are subject to the same promotion rules as prescription medicines, yet subcategories such as food supplements can be promoted through television advertisements, for instance. Ersan Küçük, general manager of Drogsan, a generic manufacturer that is exploring opportunities in the OTC market, explained the industry's frustrations: "Every pharmaceutical company tries to enter the OTC business, extending their portfolio in this area to utilize its advantages. However, without relevant legislation in Turkey, a prescription is required for most products in Turkey even if they are considered OTC in other countries. Businesses try to take short cuts by developing herbal and cosmetic products in order to avoid price control. We have tried to lobby with the authorities in Turkey but there has been no response."

There are reasons why the optimism shown by Taşpolatoğlu from Abdi Ibrahim is not shared by all of his peers. SURDER, the association that connects its 80 members with products in the OTC category, including a broad spectrum of herbal products, phytotheraphies, medical devices, cosmetics, biocidals and homeopathic products, has relentlessly acted as a lobbying body for the introduction of the legislation since the association was established in 2007. However, the lists released by the government specifying the drugs to be considered for OTC designation have oscillated between the MoH and industry, dividing the industry into two camps.

Those opposed to the introduction of this legislation are contesting the classification of certain drugs as OTC, fearing that these products will no longer be reimbursed. Smaller companies are also worried that the passing of OTC legislation will give free range to multinationals to run expensive advertisement campaigns that will drive competition away. Backlash also comes from the medical community, which worries that without supervision, patients run the risk of misusing the drugs. Authorities also warn of the increased risk that patients may encounter counterfeit drugs. On the other hand, advocates insist that liberalization of the market and active promotion will stimulate a healthy competition and eventually bring prices down. Furthermore, patients will have unobstructed access to the medicines.

Once the final categorization of OTC drugs is ready, big shifts are expected for the pharma companies currently investing in OTC lines. For instance, Ali Raif has added a new production line in 2018, and Atabay followed suit in 2019. This could also stir the interest of multinationals that have well-established products in this range and expect concrete legislation as a mitigating factor before setting foot in Turkey. Currently, multinationals are not as strongly motivated to move into this market. Ismail Yormaz, managing director of Recordati Turkey, feels that it has been too long to hold back on launching OTC products: "Next year we plan to launch a cough relieving prescription drug, for which we are developing a tablet form; this should normally be an OTC drug, but it is not recognized as such."

As the concepts of self-care, prevention and naturally sourced medicines grow in relevance, self-medication is bound to increase in importance in Turke, as it has in other developed markets. However, the infrastructure to support the OTC development must first be in place, and this includes raising awareness on disciplined and safe consumption and the installation of adequate online security systems to control illegal activities and sales of spurious drugs. Measures such as readability tests have already been introduced to ensure all medicinal descriptions and instructions are easily legible to empower consumers to make well-informed decisions without the need of medical assistance.

Since the introduction of the mandatory discounts, out-of-pocket payments have fallen by 5%, but it is hoped that in the future pricing will relax for different product categories. Companies like Exeltis, which has juggled both types of medicines, are likely to shift strategy once again: "We have struggled with the right pricing strategy in OTC medications and trying to strike a balance between high volume-low margin products and low volume-high margin products in order to combat pricing pressures in Turkey," said Hulya Yalin, general manager of Exeltis Turkey.

Should the law be introduced and the market liberalized, the OTC drugs will then be available for purchase without prescription, taking a seat in-between pharmaceuticals and consumer goods. Although there is no guarantee the legislation will come into existence, there have been signs of a growing interest in alternative medicines, together with the exploration of Turkey's highly diverse bio-flora and its undiscovered therapeutic benefits. Moreover, Turkey has a long history in the exploration of herbal medicines, dating back to the 13th century writings of botanist Ibn al-Baitar. Looking to unwrap some of its hidden potential, President Erdoğan inaugurated the first dedicated phytotherapy, or modern herbal remedy center in 2015. The center's mandate is to investigate medicinal plants to extract and develop formulations for use in the pharmaceuticals, cosmetics and food industries. ■

Traditional Herbal Medicine in Turkey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IITÇ

Doğan Taşkent, Board Member
ATABAY İLAÇ
Prof. Dr. İ. İrem Tatlı Çankaya
HACETTEPE UNIVERSITY FACULTY OF PHARMACY – PHARMACEUTICAL BOTANIC

Traditional medicine (TM) is an important part of health services. In Turkey traditional medicine is termed traditional and complementary medicine (TCM). TM has a long history of use in health maintenance and disease prevention and treatment, particularly for chronic diseases. The WHO Traditional Medicine Strategy 2014–2023 was developed and launched in response to the World Health Assembly resolution on traditional medicine (WHA62.13). The strategy aims to support member States in developing proactive policies and implementing action plans that will strengthen the role traditional medicine plays in keeping populations healthy.

In many countries around the world plants have been used extensively in traditional food forms, either as food supplements or as herbal medicine. According to WHO reports, 80% of the population in developing countries use traditional herbal medicines for basic health needs. In some countries where it is difficult to reach the physician or medication (such as Africa, some Asian and South American countries), plants are used as folk medicine with traditional information and have therapeutic value comparable to conventional medicines.

Since the recognition of herbal medicines has also increased in European countries, EMA (European Medicines Agency) has initiated studies to harmonize the assessment criteria applicable to the member states for herbal medicines. HMPC (Committee on Herbal Medicinal Products) was established to make arrangements on herbal medicines.

In Turkey the preparation of herbal medicinal products as well as the evaluation of herbal medicinal products on the market is conducted by the Ministry of Health and Ministry of Agriculture and Forestry according to their own legislation. The Ministry of Agriculture and Forestry is responsible for food supplements, on the other hand, licensing of traditional herbal medicinal products with protective and therapeutic effects on human health is done according to the "Traditional Herbal Medicinal Products Regulation" published by the Ministry of Health on October 6, 2010.

Nowadays, declarations about the medical effects of herbal products, increasing consumer interest in natural treatment methods, the inability of modern treatment systems to treat certain diseases, health consciousness of the elderly population, thoughts that natural treatment methods are safer are the main reasons to choose treatment using plants in Turkey. However, a report published by the World Health Organization stated that, in many countries where herbal medicine is traded, legal regulations are not sufficient and quality control, efficiency and safety studies of these products are not performed. This may pose a great danger to public health.

The products to be used for medical purposes must carry the criteria of quality, efficiency and safety. A product can become "medicinal" only after completing these criteria. Therefore, the dose required for effective treatment administration should be continuously provided. The most important difference between the therapeutic and lethal effects of a substance is its amount. So the dose is very important in herbal medicine products. The amount of active ingredient in medicinal plants must be uniformly provided in each pharmaceutical form. In addition, for the sustainability of the efficacy of the products, it is essential that the plant extract should be standardized and the stability of the product, as well as the pharmacological, toxicological data and clinical findings, should be obtained.

The plants and herbal medicinal products produced must be of pharmacopoeia quality and world standards. Many species that are accepted medically in the world, whose efficacy is proven and included in pharmacopoeias and monographs, grow naturally in Anatolia and some of them are cultured. Next to the rich flora there is manpower, knowledge and technology to produce herbal products starting from the field and to develop new products and present them to the market. On the other hand, it is of great importance that future generations are protected in order to protect biodiversity and natural resources.

Institutions like TAGEM (General Directorate of Agricultural Research and Policies), BACEM (Balıkesir Farmer Education Center), TİGEM (General Directorate of Agricultural Enterprises) Hacettepe University, Gazi University, Marmara University, TÜBİTAK MAM, make great contributions to traditional herbal medicinal products and their development in Turkey. ATABAY currently focuses on setting up interactions between academia and governments to foster sustainable production on bioactive metabolites derived from traditional herbal medicinal plants by using modern biotechnological approaches. ■

Made in Turkey

THE LOCALIZATION POLICY AND ITS EFFECTS

Over 80% of Turkey's drugs are made in-country; however, these products tend to be below-value generics. Monopolized by foreign companies, the high-value originator market brought US$3.5 billion in sales in 2018, while the generics market of local companies accumulated only US$1.5 billion, despite producing more than double the volume. Multinationals are backed by offshore production facilities and large product baskets, which allows them to accommodate to the latest trends in demand in Turkey more easily, at a time when local companies need to make careful decisions about what and how much of a product should be manufactured. Foreign companies are able to better control the cost of the original drugs, as well as recoup costs from operations in higher-margin countries. In order to rebalance the dynamic between local and foreign companies, Turkish authorities resorted to a localization measure that will force multinationals to bear more of the risks of production.

The localization policy, launched in 2016, demands that all drugs reaching the domestic market and that can be feasibly produced in Turkey must be produced in Turkey. This is known as the "localization requirement," and it entails a ban on imported drugs and an implicit request for technology transfer. Should the localization requirement not be fulfilled, Turkish authorities retain the right to reject the drugs from the reimbursement scheme, effectively driving the drugs out of the market. Multinationals are thus forced either to invest in a local manufacturing plant or to outsource to local manufacturers. Özdemir Şengören worked most of his life for multinationals, before taking a general manager role at local producer Farmatek a year and a half ago. Having sat at both sides of the table, he believes Turkey needs both the originator and generics drugs to achieve balance: "In a 100% reimbursed market, everyone has to make sacrifices for the market to remain sustainable," he said.

Local pharma must encourage the presence of multinationals whose original drugs are the very reason of existence for the generics (manufactured by local companies); international companies, on the other hand, are expected to comply. The policy has drawn the attention of the EU, which made a formal complaint against Turkey to the WTO in April 2019. Opening an active dispute called 'Certain measures concerning production, importation and marketing of pharmaceutical products,' the EU alleges that the localization policy is inconsistent with the GATT 1994 Article III in that the localization requirement, together with the technology transfer requirement and the import ban on localized products, treats imported drugs less favorably than products of national origin. Moreover, the EU argues that Turkey has failed to publish terms and conditions of application of the localization measure, which impedes governments and traders to respond to it adequately. The consultations were joined by the United States, and a panel was established in September 2019 involving Brazil, Canada, China, India, Indonesia, Japan, the Russian Federation, Switzerland and Ukraine as third parties. Until a decision is taken, the localization drive remains uncertain.

Even if the localization project passes this legal challenge, the policy risks being seen as a forceful, protectionist exercise that will cause the country to lose its attractiveness in the eyes of the international community. "In my opinion, the localization project is a badly applied good idea," said Deniz Demir, general manager of Dem İlaç. "The MOH should be more lenient if the goals of the localization policy are to be accomplished without being seen as too autocratic. The localization policy should be carried out in a way that speaks positively of Turkey and makes the country more attractive for investors and multinationals alike," he concluded.

Turkey is not the only country to have decreed localization efforts. Russia, Brazil and even the United States have over the years adopted policies aimed at bolstering local production over imported goods. Pointing at the United State's long-waged tariffs battle with China, countries around the world see a precedent to protect domestic production at the risk of being accused of protectionism.

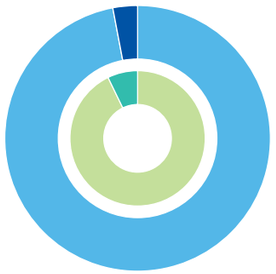
In the meantime, multinationals operating in Turkey have few options but to support the policy. "We believe that localization is an important initiative for local pharma industry producers and the country's economy. Today, 90 of every 100 boxes of Daiichi Sankyo's products that reach patients in Turkey are manufactured in our country," shared Fatih Yedikardeş, general manager of Daiichi-Sankyo, a Japanese global pharma innovator with a competitive edge in oncology.

Sanofi, which has invested over US$1 billion in Turkey, does not relate its investment to the localization policy: "Irrespective of the policy, we have put our faith in Turkey", said Cem Öztürk, general manager of Sanofi Turkey.

While the policy may be seen to pin local companies against multinationals, Ayça Sezer, business development director at Santa Pharma, believes the policy has brought the market closer together indirectly: "In the past, collaborations with foreign players were not easy, but today the industry is more united," she said.

Before this policy was enacted, multinationals had few reasons to partner with a local player, but the new measure makes

IMPORT PRODUCTS, 2016



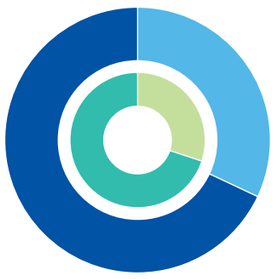
Breakdown of Sales Value

Generic	3%
Originator	97%

Breakdown of Unit Sales

Generic	7%
Originator	93%

LOCALLY-PRODUCED PRODUCTS, 2016



Breakdown of Sales Value

Generic	68%
Originator	32%

Breakdown of Unit Sales

Generic	70%
Originator	30%

local manufacturers indispensable in helping multinationals "localize" their products, thus increasing the traffic of partnerships. For example, Daiichi-Sankyo produces 90% of its Turkish products domestically through local manufacturer Abdi Ibrahim. However, Abdi also outsources some of its products to French multinational Sanofi. In turn, Sanofi works with Birgi Mefar, a local contract manufacturer, for its parenteral line. Connecting Turkey to even further links, Sanofi also produces the full portfolio of German big pharma Bayer.

Nonetheless, these collaborations do not mean that all players are equally advantaged. Pharma companies without manufacturing facilities are concerned by the policy. Platin Kimya, a family-owned company that imports APIs and formulations, almost closed its pharma business when the policy was enacted: "At that point, we could have left the industry, but we decided to stay in the business and appeal to local CMOs of high quality," said Esra Saraçoğlu.

Importers and distributors already act as a third party in the supply of medicines, but with the introduction of the localization requirement, they will need to involve a fourth player in the form of a CMO.

In fact, the undeniable winners of the situation are the CMOs, as the best positioned to profit from demand in toll manufacturing. Faik Somer, CEO of Birgi Mefar, the oldest and largest contract manufacturer for parenteral solutions, explained the advantages brought by the policy: "With a successful marriage between local players and multinationals more doors are opened to use our facility for different purposes. For instance, in our partnership with Sanofi we started with the local business, but the partnership created more opportunities in other businesses too."

The CMO business is expected to be so successful that some fear the localization measure will make Turkey a hub for contract manufacturing, which would impede its ability to innovate and add value. As ownership of a manufacturing plant becomes less attractive due to the large bills incurred, CMOs have the ability to keep costs to a minimum by optimizing processes and streamlining production; moreover, with the growing demand in specialized drugs such as injectables, it becomes inefficient for companies to continue specific lines alongside other products when they can be produced in bulk by CMOs.

Taking note of the growing opportunities in this segment, new generic entrants like Pharmactive are dedicating large portions of the business to toll manufacturing. The localization measure is likely to play an important role in the diversification of business models as the interests of multiple players intersect and local producers seek to fill their capacities. Producers will be more inclined to complement their manufactured drugs with in-licensed, locally produced drugs through partnerships with global players while hoping that the closer partnerships will also result in more out-licensing agreements. Farmatek, a former drugs importer that recently opened a manufacturing facility, incorporated a hybrid business model, including the offer of CDMO services in order to maximize the utility of its lab.

Perhaps the greatest advantage of the localization policy is not reflected in corporate balance sheets or in balancing the trade deficit, but rather in the technology transfer that will bring much needed expertise into the Turkish market. Multinationals have agreed to produce a higher proportion of their products in Turkey: Recordati produces 96% of its portfolio in the country while Sanofi produces about 86% locally. The remaining fraction is produced outside of Turkey because the technology is still unavailable in the country. The vague instructions on when and how the technology transfer should be realized leaves room for interpretation. Fatih Yedikardeş, general manager of Daiichi-Sankyo, dares to believe that localizing R&D could be the next relevant step in localization efforts.

Given the newly forged collaborations created in manufacturing it is not implausible that similar partnerships may migrate to the R&D front – not only in transferring knowledge, but also in joining forces to develop the next generations of medicines. However, for partnerships to progress into R&D projects requires time for trust between local and global partners to further mature.

By its name, the localization measure is a reaction to the globalization processes that have shaped world economies. More than the anti-globalizing message that its name conveys, the localisation policy could turn into a precursor for Turkish manufacturers to reach global circles: "The localization decision was a great opportunity for companies to prepare themselves for the global arena. Through this policy, contractors increased the knowhow of high technology manufacturing processes, invested in new manufacturing lines for high technology products and increased manufacturing capabilities. It provided the chance to see the culture and approaches of global companies in GMP and GLP," said Mehmet Asri, general manager of Polifarma.

The localization policy has left its marks on the broader value chain, including local companies. Currently in phase two, the policy is being piloted before more details are clarified, which leaves both indigenous and foreign pharma companies unsettled. If successful, the localization measure could set the market on a course for greater consolidation. Acquisitions of local companies have been the entry point for multinationals into the country, like Exeltis buying 100% shares of local Embil. The latest acquisition occurred when local chemicals distributor Ekin Kimya was bought out by multinational Azelis, a transaction approved in December 2019 by the competition authorities. If local manufacturing becomes an absolute requirement, it would make sense for large international players to take proprietorship over local production. However, many questions remain, including whether the localization measure will bring the intended advantages, and, more crucially, whether there will be any unintended consequences to address? ■

Faik Somer

CEO
BİRGİ MEFAR İLAÇ

Could you briefly introduce Birgi Mefar?

Birgi Mefar Group is the oldest CMO in Turkey, founded in 1963, and the largest by market share. Starting with the production of ampoules, Mefar shifted in time to being a contract manufacturing organisation with a specialisation in ampoule filling, and now includes BFS (blow-fill seal), PFS (pre-filled-syringes), vial, lyophilisation (vial & ampoule) and packaging in its products and services. A significant milestone in the company's evolution has been the change in management to align it with the vision of making Birgi Mefar Group a global player in nearby geographies, namely Europe, Middle East and Central Asia.

What is your insight regarding the main growth pillars in this sector?

The CMO business is growing at a fast pace. Globally, the CDMO business is close to US$10 billion dollars, with a growth rate of around 5-6%. Within this healthy market, the sterile manufacturing sector has enjoyed the highest growth, almost 30%—a rate it has maintained for five years. Injectables and biologics are the main drivers, and that's why we are looking to take more market share in these areas. Five years ago, we started in vaccines (PFS-prefilled syringe business), and we are now the premier CMO in vaccine production in Turkey. We manufacture vaccines for multinational companies, having produced more than a hundred million doses of vaccines over the course of the year, without fault.

How has the localisation policy impacted your partnerships with foreign players?

Although we're geared towards multinational companies, the policy gives us, as a local player, a tactical advantage: we become the first door to knock at for services in this sector. With a successful marriage between local players and multinationals, more opportunities arise to use our facility for different purposes. For instance, in our partnership with Sanofi, we started with the local business, but the partnership created more opportunities in other businesses, for which Turkey could become a hub. Biosimilars are a very different business. In this sector, it is not practical to run a factory just for one or two products, and a CMO becomes optimal to finalise registration or to make the commercial product.

How does Birgi Mefar's business prioritise between domestic and export markets?

Our priority will gradually shift to the global arena. Today, the proportions are at 40% exports and 60% domestic. Within three years, we expect these percentages to reverse, with a greater foothold in export markets.

What are your predictions concerning the pharma and biopharma sector and what conditions would allow this industry to take off fully in coming years?

To answer this, I would like to return to basics before talking about biologics, which are the new "sexy" trend in today's market. In fact, we need to step back even before addressing R&D, to consider "R" and "D" separately, and only then the "B", of biologics. For "R", the government needs to look into legislation to bring universities on board, a model which has proved successful in other countries. The appropriate commitment to research can be realised by creating a three legged support, between the government, universities, and the pharmaceuticals industry. Delivering this support is a challenge, but it does not require vast resources. Once completed, we can move to "D", which is the most expensive part. Money is available for research, but there are legal loopholes which mean that money can only go into the universal budget in the university, limiting the possibilities for bilateral collaboration between a professor and an industry player. There is an drain of talented people wanting to do research, and it is a shame to be missing out on the potential of their expert input due to this capital barrier.

Would you like to share your vision of how Birgi Mefar may develop in coming years?

We aspire continuously to seize a bigger market share from the growing CDMO business worldwide. To do so, we invest in building capacity and, equally important, we invest in people. Quality is the game, and we make sure that Mefar is correspondingly associated with quality. We are a pure CMO, and we will stay a pure CMO to secure a trusted niche, as well as a differentiation point for our clients. This focus will underpin Mefar's drive to become a global player holding the Turkish flag in the global marketplace. ■

İsmail Yormaz

General Manager
RECORDATI İLAÇ

Recordati has made important acquisitions in recent years. How do these acquisitions underscore the company's strategy in different therapies?
Last year, Recordati completed the acquisition of Natural Point in Italy, an entity dedicated to food supplements. Recordati also bought French Tonipharm, increasing its portfolio in OTC drugs. Besides these examples of inorganic growth, Recordati is actively expanding its portfolio through buying marketing rights for different products, especially in the treatment of rare diseases, a segment in which Recordati is recognized as a global leader. In the first half of 2019, Recordati acquired the exclusive licence for Juxtapid in Japan, as well as the global rights for Signifor and Signifor LAR from Novartis. One of Recordati's strongest areas of operation is in orphan drug acquisition initiatives; while specialty and primary care divisions, together with the OTC business are important segments, Recordati remains mainly involved with orphan drugs in the treatment of rare diseases, for which we boast a presence on all continents.

How would you describe the climate for pharmaceuticals in Turkey today?
Political tensions increased in Turkey in 2016, along with a set of other issues which hit the economy hard. Today, Turkey continues to be a significant economic player especially in comparison to its immediate neighbors, but the reality one has to be reminded about is that Turkey's geographical position is not an enviable one like Belgium's. Many people talk about the advantages of Turkey's location as a bridge between civilizations, and of course this is an asset, but nonetheless this location also puts Turkey in a delicate situation. Its proximity to Russia, the Middle-East, Europe and Africa creates tensions that are beyond discussions about pharmaceuticals, but which nonetheless impact our industry. I maintain my position that the years between 2009 and 2014 were the worst for the pharmaceutical market in Turkey. The negative structural effects of the pricing regulations are still felt in the market today.

What mechanisms have Turkish pharmaceutical players developed to respond to price pressures?
In the current context, a drug (in the cheapest EU country) sold for €10 will be valued at approximately €2.97 as a reimbursed product in Turkey, based on the official exchange rates and the National Health Count System Discounts. This system puts immense pressure on the pharmaceutical industry, whose ability to innovate and make investments is curtailed. However, pharma players have evolved; these pressures have compelled the industry to innovate and create cheaper and more affordable products. The affordability of Turkish drugs is very attractive to neighboring markets that struggle with their own economic challenges. The pharmaceutical industry of Turkey has earned the designation of a producer of both high quality and affordable drugs.

What are Recordati Turkey's main pillars of growth?
Recordati is currently producing more than 96% of all its Turkish-consumed products in facilities based in Turkey, which makes us a globally recognized organization, well attuned to the localization policy. In the last three years, we have launched nine new pharmaceutical products, four of which are new chemical entities, while the remaining five are different formulations from existing chemical entities. Recordati's Çerkezköy facility is also in the process of obtaining its GMP certifications from different countries for future export possibilities. Besides the Turkish MOH GMP-Approved Certification, Recordati also obtained its EU Certification for their semi-solid products from the Danish governmental authority. In addition, our facility received the GMP approvals from the authorities of Azerbaijan, Kenya and Libya. ■

Many people talk about the advantages of Turkey's location as a bridge between civilizations, and of course this is an asset, but nonetheless this location also puts Turkey in a delicate situation. Its proximity to Russia, the Middle-East, Europe and Africa creates tensions that are beyond discussions about pharmaceuticals, but which nonetheless impact our industry.

Hülya Yalın

General Manager
EXELTIS İLAÇ

Could you provide a brief introduction to Exeltis' operations in Turkey?
With its young and aging population Turkey has been an important geography for all healthcare players, and Exeltis entered the Turkish pharma market in 2014 by acquiring Embil, a local Turkish pharma company which had its own manufacturing plant. Currently, strengthening our position in women's health and expanding into the respiratory market are the top two priorities of Turkey Exeltis' operation. We are trying to strengthen our current portfolio's brand equity in the market and, in parallel, we are searching for new investment areas, in specialty care and primary care, for sustainable growth over the mid- to long-term in this attractive market. R&D is another key focus area and we are working on two new projects that will target domestic as well as international markets.

Could you elaborate on Exeltis' product mix and the key therapeutic areas the company serves?
Our portfolio offers a diverse range of healthcare solutions to women of all ages, especially from youth to menopause. We aspire to be a strong partner of women for a lifetime during their health related needs, and we are proud to support them with our exceptional product portfolio, the majority of which are produced in our local facility with the highest technological standards. Some products such as hormones and food supplements are imported from our production facilities in Spain. Beyond our strong women healthcare portfolio we are focusing on key therapeutic areas like respiratory and pain which are important cornerstones in our organization for future growth.

What are the advantages of being a manufacturer in Turkey?
There are four major advantages in being a manufacturer in Turkey: Optimal geography, high quality standards, a wide talent pool and competitive cost structures.

Could you elaborate on Exeltis' R&D efforts and how you differentiate your products?
Besides our manufacturing facility, Exeltis Turkey has its own R&D facility. Our R&D team is developing two strong products that will be made in our facility in the near future. We are moving confidently towards our vision of becoming an end-to-end pharmaceutical manufacturer.

What challenges do you face in the Turkish market?
One of the key challenges is the volatility of the Turkish Lira, its effect on the Reference Country Pricing system that is applied to all reimbursed products in Turkey and, in parallel, its impact on the purchasing power of the consumer.
Another challenge for our company is reaching wider stakeholder target groups spread all over the country. To overcome this difficulty we are focusing on reaching stakeholders with new go-to-market models, "going digital" via multichannel engagements.

How will you reduce the risks posed by currency volatility in the future?
During the devaluation period, we experienced another advantage of being a manufacturer. 25% of our sales comes from exports, which gave us pricing opportunity during the economic turmoil in 2018-2019. To a certain extent, we could balance our loss stemming from increased cost of imports with our gain from exports. This brings us to our second strategy to cope with the currency volatility risk; increasing the share of exports so that we can reach an optimal balance between import and export products for a sustainable future of our company and further investment in Turkey.

What are the ambitions for Exeltis in Turkey over the next five years?
Exeltis is dedicated to be in top 50 pharmaceutical companies within Turkey in five years. Our growth rate of 45% -whereas the market performed at 34%- tells us that we are on the right track to realize our objective. However, are not satisfied with our current pace. We have identified three pillars of growth which will leap-frog Exeltis in the upcoming period. The first is maximizing our existence in women's health area and strengthening our position in respiratory diseases. Secondly, we will increase our effectiveness in leveraging all our capabilities including R&D pipeline, import and export. Finally, we plan to enter new specialty areas by investing in specialty and primary care products. During this organic and inorganic growth stage of the company, we are very proud to create job opportunies to many by trippling the size of our field force. We believe that this mutual benefit between Exeltis and Turkey will strengthen our bonding with patients and improve the lives of millions of people. ■

Murat Akturk

General Manager
SANOVEL PHARMACEUTICALS

Can you give us an overview of Sanovel Pharmaceuticals and its recent milestones?
Over the years, the company has shown strong growth backed by powerful brands, a highly efficient, optimised field force with a Rx/pharmacy balanced approach, a strong pipeline management yielding successful first-to-market generic launches as well as competent change management and leadership.
In 2019 Sanovel's production facility obtained FDA approval, which is a major milestone and will allow us to export our products to the United States from the beginning of 2020.

Sanovel decided not to in-license products that were not 100% in-house. What are the advantages?
Full ownership of products means high margins with no royalties. Sanovel's first-to-market generic strategy is backed by unique intellectual property and R&D activities, which are key differentiating factors and have led to lasting competitive advantages and strong brand equity.

What are the key therapies you are targeting?
We have a strong presence in core therapeutic areas including anti-ulcerants, cardiovascular systems, antirheumatic systems, muscle relaxants, antibacterials, anti-diabetics and anti-epileptics. We are enlarging our portfolio in favour of chronic therapeutic areas such as anti-thrombotic agents and anti-cholesterol drugs. And also, as a branded generic company, we are developing new formulations and combinations of existing products in different pharmaceutical forms with our world-class manufacturing capabilities.

Could you elaborate on Sanovel's presence in export markets?
Sanovel leads the way in acute and chronic markets in Turkey and always tends to internationalize and globalize its business activities. The company has been exporting products to local regions such as Turkmenistan, Azerbaijan, Kazakhstan and other CIS (Commonwealth of Independent States) countries and operating with its own marketing teams till 2015. Then we changed our strategy and started working with distributors in those countries. Sanovel, as a branded generics company, wants to be a player in global markets and the emerging markets in particular. In 2019, we partnered with Abbott Laboratories in most of the CIS countries.
Our current portfolio and innovative pipeline match most of the potential export markets and registrations are in progress in countries such as Spain, Thailand, Vietnam, Malaysia and sub-Saharan countries.

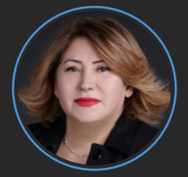
How does Sanovel fare against foreign competitors in these markets of operation?
Competition is important because it compels industry to provide higher quality goods and services at lower prices. We know that pharma companies should tailor their strategies to fit local markets.
Sanovel pursues a cGMP quality management system in compliance with international standards and operates a fully integrated manufacturing facility in accordance with EU GMP procedures. All products manufactured comply with applicable standards, including EudraLex – Volume 4 GMP guidelines, FDA guidelines, PIC/S directives, World Health Organization recommendations and various ICH standards, thus creating world class quality products with affordable prices.

How many countries is Sanovel presently trading in?
Currently we are trading our products in 10 countries mostly in the local region. Since the beginning of the company our major focus was always the Turkish pharmaceutical market. For the last five years we are focusing on potential and strategic export markets and fully working on registration processes in new countries. Apart from CIS countries, Albania and Iraq, all our eyes will be on US market in 2020.

What would you say is Sanovel's strength in obtaining patents rights?
Sanovel has a pioneering track record of IP protection activities among Turkish corporates. According to the Ministry of Industry, Sanovel is the first firm in terms of IP competence among all government certified R&D centres listed in Turkey. Sanovel has been Turkey's most prolific national patent filler in the pharmaceutical industry since 2011.

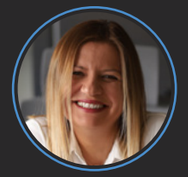
Do you have a final message for our international readership?
Turkey is a natural bridge between both the East-West and the North-South axes, thus creating an efficient and cost-effective hub to serve major markets. In such a geostrategic location, providing world-class products at affordable prices is the way to internationalize and globalize our business. ■

INDUSTRY VIEWS ON LOCALISATION



"The localisation policy has helped us obtain more contracts with customers because small and mid-sized companies who relied on imports are now required to produce in Turkey, and without the technical production and R&D facilities, these companies reach out to both CMOs and CROs to execute the dossier for them."

- Şirin Deha, General Manager, Era Pharma

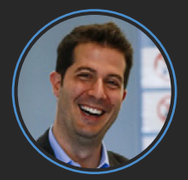


"With the localisation efforts made in the industry, international companies are shifting their manufacturing sites to Turkey. Santa Farma would like to position itself as a production hub within this process, as the owners of some of the most productive facilities in the country."

- Dr. Ayça Sezer, MD Corporate Business Development Director, Santa Farma İlaç

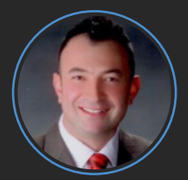
"Within the current framework of reimbursements, the government is the main player, purchasing more than 85% of the total product output; naturally, the authorities would like to protect local production. When the localisation policy was introduced, we were put at a disadvantage and had to evaluate our commitment to staying in the business."

- Esra Saraçoğlu, General Manager, Platin Kimya



"As an intermediate to our clients, we offer local companies more freedom, independence and flexibility. For the country, it could well be said we are bringing a platform for localization in Turkey. The company can contribute in making localization become a reality, provided that the local industry also gives us the chance to do so."

- Cem Erdem, CEO and co-founder, Florabio



"In my view, the localisation project is a badly applied good idea- it is not that I believe the MoH should be stricter, but on the contrary, it should be more lenient if the goals of the localisation policy are to be accomplished without being seen too autocratic. At this point, the localisation policy is seen as a dictation, which I believe may lead to unforeseen circumstances in the longer term."

- Deniz Demir, Chairman, Dem İlaç

BIOPHARMACEUTICALS

» I like to think of the world as a single place, but there is a misconception that nothing innovative can come out of an industrial country like Turkey, that the research and ideas here are not developed enough to result in original research. This is not true. We have educated young investigators and strong infrastructure, but we need to organise these assets and bring together universities and industry players. «

- Prof. Dr. Tanıl Kocagöz,
Head of Department of Medical Microbiology and Biotechnology,
Acibadem University

Image courtesy of Florabio

Large Molecules

THINKING BIGGER: THE TRANSITION TO LARGE MOLECULES

The Turkish pharma industry is on the eve of a rebirth as it seeks to grow a biopharma component. Representing 17% of the total prescriptions share in Turkey, the biopharma sector grew by 30% in 2018 to reach US$859 million. More impressively, the biosimilars market rose by 42.2% in the same year to a total value of US$47.5 million. However, the 250 biologics and 83 biosimilars currently on the Turkish market are mostly imported products, putting a significant burden on the healthcare budget.

Although the localization instrument may prove useful in obliging local production for chemical drugs, this is not a practical option for biopharma. International biotech companies would be unable and unwilling to make the transfer of sophisticated technology to Turkey. As such, the best alternative left for the government is to incentivize the creation of a local biopharma sector. Despite the heavy task at hand, Turkey puts its faith in its potential: "We believe the biopharma industry will be among the first three to strengthen the country's economic power," said Professor Berrin Erdag, chief senior researcher of state agency Tübitak.

The first isolated attempts at developing biopharmaceuticals took place in the early 2000s. However, systematic efforts and the de facto birth of the industry began in 2013, when the government made substantial funds available for this sector. Organizations like Tübitak, The Scientific and Technological Research Council of Turkey, and TÜSEB Health Institutes of Turkey became prominent actors in facilitating grants to the sector for both early and later-phase development, including clinical studies. Nobel, Atabay, Deva and Ilko were the first recipients of non-refundable money granted to encourage the first steps in building biotech capabilities and other companies followed suit. Centurion made a US$37 million investment in 2015 to build a biotech plant for the development of biosimilars in Ankara.

The foundation of Turkish biotech differs greatly from other countries. A young industry worldwide, biotech is typically made of young SMEs stemming out of campus-based research labs. By contrast, the Turkish biopharma component is not an endogenous new segment, but an additional component grown by the existing pharma businesses. The chemical pharmaceutical companies that accepted to grow these new legs were incentivised by both the funding put at their disposal, as much as by upcoming limitations in chemical drug production. As fewer original chemical drugs are expected to lose patent in coming years, the biopharma segment counteracts with considerable opportunities. Prof Berrin Erdag, at Tübitak Mam Generic Engineering and Biotech Institute (GEBI), believes 30 out of the 50 best-selling molecules will be biopharmaceuticals.

Some pharma companies have been quick to jump on the opportunity, replicating the power structures they established in the traditional pharma industry. A market leader in traditional pharma, Abdi Ibrahim proportionately invested in a large biotech drug facility, AbdiBio, in 2010: "Biologicals will shape the future of the pharma industry, and I believe companies should be investing so that they are not left behind," urged Süha Taşpolatoğlu, Abdi's CEO.

Whether Turkey's investment in biopharma is too hasty or not fast enough is a matter of debate. Professor Tanıl Kocagöz of Acibadem University believes Turkey has awoken to the importance of biopharma very late, but there is still a chance to catch up. Creating a biopharmaceuticals ecosystem is a lengthy process; while building a manufacturing site may take as little as 18 months, the development of a biosimilar molecule is a much longer commitment, stretching over years. Süha Taşpolatoğlu provides insight into this timeline: Abdi Ibrahim, employing more than 4,500 people worldwide, expects to have its first fill-and-finish product ready in 2021 and the first biosimilar in 2027. Going as far as developing original molecules is a dream so far not thought of.

Five years ago, there were more than 19 companies making investments in biotech and today, 41 projects, including two reference products are bustling in the pipeline and expected to launch by 2024. While some have jumped head-first into the promising sector, other players have taken a more conservative stance. Philipp Haas, chairman of Deva, one of the first recipients of funding for biotech, is more cautious about the future: "Biopharma is a challenging arena that one cannot rush into," he explained.

Even if the government has kick-started construction of facilities, many of the players with hopes in biotech have a long path ahead before their investments bear fruit. At this point, there are few Turkish biomolecules on the market. Turgut İlaç, the recipient of the largest governmental grant in biotech, is to market its first biosimilar in 2021. From there, the company hopes to follow with another launch yearly. However, many of the starters in biotech have still not launched any products. Large parts of the sector have resorted to importing biosimilars or conducting fill-and-finish services.

Milestones in the distribution sector of biopharma should not be undervalued though; for the first time in Turkey, local start-up TR Pharm managed to receive the first non-EU and non-U.S. marketing authorization for cancer drug Reditux of the Indian company Dr. Reddy's. A Turkish company obtaining the rights to commercialize the biosimilar ahead of European and American competitors marks a leap in the country's effort to attest itself as a capable player in the global biotech sector.

Nonetheless, without the internal production of the protein or polypeptide, the new entrants in the biopharma field remain dependent on importing these cell lines from abroad and subscribing to their suppliers' prices. Florabio is the first and only cell line and media development company to have licensed-out its products from Turkey to Europe. Owning the master cell bank is what differentiates Cinnagen, the largest biotech company in the MENA region, with 12 molecules on the market. Ferhat Farsi, CEO and co-founder of Cinnagen, had worked for many years in traditional pharma without failing to study the developments taking place in biopharma: "10 years ago, I realized there will be a big change in the pharma sector; I dreamed of implementing these changes in Turkey," he said.

Even if public money helped to jumpstart the manufacturing side, there are many missing links without which the biopharma sector will not be able to fully take shape. "In order for Turkey to compete effectively in this field, a supportive ecosystem needs to be established," said Turgut Tokgöz, SG of IEIS.

The ecosystem would involve adequate legislation to facilitate market entry for biosimilars, creating awareness about the use of biosimilars to doctors and patients, knowledge building in specialized fields together with university partners and, perhaps most importantly, investors who can provide substantial funding over an extended period. ■

BIOTECHNOLOGICAL PRODUCTS
Source: IQVIA, İEIS

	UNIT		VALUE	
	2010	2019	2010	2019
Biosimilar	**100%**	**100%**	**100%**	**100%**
Blood and hematopoietic organs	0.0%	90,3%	0.0%	57,5%
Antineoplastics and immunomodulatory agents	100.0%	3,9%	100.0%	31,4%
Digestive system and metabolism products	0.0%	4,7%	0.0%	7,1%
Systematic Hormonal Preparations *(Excluding Sex Hormones and Insulins)*	0.0%	1,0%	0.0%	3,9%
Dermatologic Products	0.0%	0,1%	0.0%	0,1%
Originator	**100%**	**100%**	**100%**	**100%**
Antineoplastics and immunomodulatory agents	6.9%	14,3%	44.2%	51,6%
Digestive system and metabolism products	51.1%	68,8%	23.8%	24,0%
Blood and hematopoietic organis	35.1%	3,7%	17.3%	10,1%
Systematic Hormonal Preparations	0.1%	1,1%	1.5%	3,8%
(Excluding Sex Hormones and Insulins)	1.9%	3,5%	4.1%	3,0%
Respiratory System	0.1%	1,5%	0.4%	2,9%
Genito Urinary System and Sex Hormones	3.3%	5,7%	3.8%	2,4%
Systematically Used Anti-infectives	1.5%	0,5%	5.0%	1,2%
Muscle-Skeleton System	0.0%	0,9%	0.0%	1,0%

Ferhat Farsi

CEO and Co-Founder
CINNAGEN İLAÇ

CinnaGen was founded in 1994 with the goal of manufacturing hi-tech products in biotechnology and related fields.

Could you tell us what led to the founding of CinnaGen İlaç in 2016?
I used to work in leading pharmaceutical companies in Turkey, particularly in chemical manufacturing. Over the last eight years, I noticed a big shift from chemicals to biological.
The Turkish biotechnology sector is on the rise and we have excellent chemical manufacturing plants. I created a strong collaboration with CinnaGen, a company that has been in biotechnology for 25 years. I partnered with them for a technology transfer to Turkey because 10 years ago the company wanted to become a leader in the Middle East and Northern Africa (MENA) region for biotechnology, and Turkey was the right place to launch that effort. CinnaGen has the largest pipeline for biotechnology worldwide, with 12 products in the market and another 13 products being launched in the next three-to-five years. Our vision is to become one of the top 10 companies in biotechnology worldwide in the next 10 years and to create an international brand for Turkey.

How has the competitive landscape in the biosimilars space evolved in recent years and how do you foresee it shifting in the future?
Currently, almost 100% of the biotechnology products in Turkey are imported and, I believe, in order to be successful in Turkey, the key is to manufacture important proteins within Turkey. Fill-and-finish is also an important process that needs to occur in the country and will require technology transfer and analytical control methods to be applied. In the last 25 years, CinnaGen has become a creator of its own master cell lines with no dependency on other companies. The most important step in biotechnology is creating the proteins or polypeptides internally, because you can then control the cost of the products. Our team has 30 people working on process optimization and increasing productivity. We are running 5,000-liter bioreactors currently and the capacity of our bioreactors is 35,000 liters overall. In biotechnological products, we are the third largest producer worldwide and we are exporting EUR 50 million worth of product to Russia alone.

How can Turkey improve its ecosystem to attract investment in biotechnology from international and domestic players?
International companies that I have spoken to are reluctant to transfer their know-how to Turkey because they have spent a few hundred million dollars on their facilities and clinical trials and do not want to share their proprietary technology. Furthermore, it is not feasible for them to shift their technology manufacturing to Turkey. As a Turkish company, our choice is either to continue importing in large volumes, which is not sustainable in the long-term, or to build our own manufacturing facilities. I would encourage local companies to invest in manufacturing to serve the local market as well as foreign markets through export, which will enable economies of scale.
As CinnaGen, we spend US$600 million for our pipeline of molecules, because you need US$30-US$50 million per molecule in development. This budget is not affordable to most Turkish companies at the moment. Recently, the government started some programs to facilitate projects for clinical trials that are near commercialization. TÜBİTAK [the Scientific and Technological Research Council of Turkey] used to find the basic science and projects in the beginning, however now they are helping existing projects reach completion. The Turkish market needs time and money to grow.

What is your vision for CinnaGen over the next five years?
My ambition is to create the biggest Turkish brand in biotechnology and a global Turkish pharmaceutical company that is capable of being in the top 10 biotechnology players worldwide. We have the market access and all the other components in place to achieve this goal. Our customers within the MENA region, South America and CIS countries are waiting for our manufacturing hub to become operational. We will be able to start the globalization of our company next year with Turkey being our hub and enabling us to create "Made in Turkey" products. Market authorization is expected in the first quarter of next year and we will aim to register our products across numerous countries. ■

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Prof. Fazilet Vardar Sukan
accompanied by researchers Sibel Çetinel and Özlem Kutlu

FV

FV: Director
SÇ and ÖK specialize in ophthalmology and rare diseases
SUNUM (SABANCI UNIVERSITY)

Can you give an overview of SUNUM and the centre's vision and purpose?
FV: SUNUM was established in 2010 as a central analytical research laboratory of Sabanci University's engineering faculty. We secured an investment of US$35 million from the Ministry of Development and the Sabanci Foundation to establish the center. The center has a very good infrastructure and the unique building is designed after the structure of the cell.
SUNUM served the Faculty of Sabanci University until 2016 when there was a state call for the development of national research centres. We made the strategic decision to apply to become one of these centers. Our application was accepted in 2017 and SUNUM is now one of the four national research centers of excellence in Turkey. Naturally, we have undergone an evolution process and we are now a self-sustained national research center with considerable funding from the state. We also attain finances from industry through contract research projects and we are also trying to create our own revenue through the development of special business models.
SUNUM was initially doing research work at early stage levels, but now we are developing projects further to prototype levels. We are aiming at doing research up to a technology readiness level of six, and we are steering towards more applied research, rather than just pure fundamental research.

SUNUM follows the "no departments, no walls" approach of Sabanci University, complementing the research expertise of different internal units and external stakeholders. Can you elaborate on this approach?
FV: SUNUM is following a very contemporary approach where the aim is to create and develop together. Societal challenges require solutions which can only be achieved by multi-disciplinary teams.

Rare diseases and ophthalmology are two of the therapeutic areas where nanotechnology is applied. Could you introduce our audience to the research carried out at SUNUM in these fields and its significance?
OK: In rare diseases, as in other conditions, we have different pathological conditions for which the exact molecular mechanism remains unknown. Most of these diseases are deemed incurable at this moment. My research focusses on understanding the molecular details of such diseases.
SC: My research is focused on diagnosing and treating diseases in the ophthalmology field. Nano-medicines have a rather universal applicability, with processes such as targeted delivery, sustained release and increasing bioavailability relevant in the treatment of any kind of disease. However, utilizing nanotechnologies is more challenging due to a significant number of barriers and we are collaborating with companies to take on the barriers. We are also focusing on tissue engineering where we are trying to regenerate tissue using biomimicked materials.

Can you give an insight into SUNUM's collaborative culture with partners in both the academic and industrial world?
FV: SUNUM's main research focus is in the nano-biotechnology space. Whatever we do has to be somehow related to nano-technologies, but we have vertical pillars in the life sciences, energy, defense, agriculture, environment, and water space. The vertical pillars and their intersection with the horizontal theme of nano-technologies, is our focus area.

Can you give some examples of successful partnerships that SUNUM has established with industry players?
FV: SUNUM has developed different collaborative models to establish good relations with industry and to secure trust and respect. The German company Merck has invested approximately € 1 million in the center and we have subsequently established a small production line for cell cultures and new molecules of pharmaceutical value. We have a SUNUM-Merck collaboration unit in the life sciences space and are progressing to a three-way partnership model, which include SUNUM, industry and pharmaceutical companies, to develop novel molecules.

Do you have a final message for our global readership?
FV: Turkey has significant potential, especially with regards to the country's highly qualified R&D workforce. The country also has quite good infrastructure which makes us competitive by international standards. We must continue to create a win-win environment through partnerships and collaborations, nationally and internationally. ■

Prof. Dr. Mehmet Öztürk

Director and Research Group Leader
IBG (IZMIR BIOMEDICINE AND GENOME CENTER)

Could you provide an introduction to the IBG since laying the first pillars in 2015?
We worked very hard for the last five years and, in a short time, we have accomplished important milestones. IBG is the largest life sciences center of Turkey. By the end of the establishment phase which is likely to last for another two years, IBG will employ 500 researchers and staff. Our focus is on life sciences and, specifically, on biomedical and genome sciences in relation to the pharmaceutical industry. We are becoming a hub for development of new biopharmaceuticals with four biosimilars in our development pipeline. In addition, our facility can support cell line generation and downstream process development with analytical capabilities. We are establishing a GMP certified therapeutic cell center. Furthermore, next year we plan to start our first original pharmaceutical development project on monoclonal antibodies. Taken to competition, this accomplishment will make IBG one of the first centers to include original molecules in our portfolio across Turkey.

Could you describe what was the core vision in setting up the center?
The IBG center is a national research center and this concept is completely new for Turkey because thus far R&D had been conducted in universities exclusively. In 2018, the government created national centers for the first time in Turkey and we represent one of these novel entities. Our vision is to create a center where we can produce data through research and transfer this knowledge into profitable technologies. In the long term, we hope to excel in the fields of cancer and rare diseases by developing our treatment capacities and becoming a center of excellence.

What does Turkey need to further develop its ecosystem in biotechnology in line with the opening of centers such as IBG?
What our scientists and engineers develop in the lab does not get translated to industry, intercut by missing links in the sector. We need to bridge these two realms and create mechanisms that will help the transition from laboratory to industry. The government is doing some work towards this goal by supporting capital venture funds that invest in startups focused on high technology platforms within biopharmaceuticals. Even though we benefit from strong infrastructure, the problem is that Turkish investors are risk averse and unwilling to commit their capital for longer than three to five years, which is not conducive to startup culture-which requires 10 to 15 years to see a return on investment. This short-sighted vision and culture is the big obstacle.

Could you give some examples that show IBG's successful collaboration with industry partners?
We have four biosimilars in our pipeline. The first product is developed for a domestic pharmaceutical company. The other three biosimilars are developed together with an American startup company. Together we combine technological skills and heavy research infrastructure.

Could you give us an insight into IBG's core areas of research and its ambitions in these fields?
We have two key focus areas: cancer and rare diseases, also called orphan diseases. For cancer treatment, our approach is to discover new targets and develop tools to facilitate the development of new drugs. Instead of working on chemicals, we prefer to work on proteins and therapies involving recombinant DNA technology. A typical example of our approach is to first discover extracellular proteins involved in resistance to drugs and then develop monoclonal antibodies against such proteins to block their contribution to resistance. We test such antibodies initially in vitro under laboratory conditions, then in animal models of human cancers.
For rare diseases, we have three aims. The first is to explore children's rare diseases and identify new causative genes. The second is to develop tools for genome-based diagnostics of these diseases. Our third aim, which is a long-term goal, is to develop molecular and cellular therapies against selected rare diseases.

What would you identify as being a key challenge for biotechnology in Turkey?
Our research is heavily dependent on imported reagents and other products. Unfortunately, because of complicated regulations for import, the process is very slow and expensive. This has a very bad effect on our speed of product development. ■

Opportunities and Legal Loopholes in Biosimilars

Between executing simple fill-and-finish processes and the more far-fetched hope of developing originals, Turkish companies' best chance is in biosimilars. Producing a biosimilar follows a comparable pathway to that of a biologic, with the significant exception that the development phase can be up to 80% cheaper. Zafer Toksöz, CEO of Arven, spelled out this compromise: "Realizing that biologicals are the future of the industry, but without the capital to invest in developing new drugs, we decided to focus on the biosimilar space."

Like Arven, many of the companies active today in the biopharma space are developing biosimilars. Murat Barlas, chairman of pharma importer Liba and President of the Turkish Biopharmaceuticals Platform (TBP), believes the biosimilar market is already too crowded, even before the products are launched.

Often thought of as the generics of large molecules, biosimilars actually bear little resemblance to small molecule generics in terms of the physical structure and manufacturing processes, though a comparable pricing philosophy applies. Since the first FDA approved use of recombinant human insulin in 1982, the growth of biopharma has outpaced classic pharma as the new category of medicines were not merely controlling the symptoms of diseases, but also intervening in the functioning of the body's immune system. The business model of biosimilars diverges from the "one size fits all" generic model, in which a blockbuster drug is used for long periods by a large population segment. A biosimilar, like a biologic, could potentially cure a disease, shifting the business model to more personalized treatment, or what has gained currency as "precision medicine."

However, the pricing relationship between an originator-generic applies to the biologic-biosimilar duo. The innovator molecules, whether small or large, occupy a privileged position rewarded through higher prices for a given time, until competition from imitator drugs can bring prices down. Nevertheless, the extent to which these prices are brought down is a sensitive consideration, especially in biopharma, because of the need to recoup larger investments. With the current reference Turkish price system in use today, prices are brought down by 30% to 40% of the real-market price of the product. The pricing roadmap can get even blurrier in terms of the competition with originators. Multinationals with the ownership of the original drug can reduce prices by up to 70% to obtain tenders, which effectively closes the market for biosimilars. Without a more defined legal framework for biosimilars, the message for investors in this space is a conflicting one.

To stay competitive biosimilars producers are forced to drastically reduce prices, which saves the government significant money. For instance, high-tech drug importer TR Pharm recently secured a biosimilars tender in which the Turkish government saved 400 million TL against the originators price. Besides sparing public finances from high expense bills, biosimilars bring much needed treatment for patients who do not have access to biological drugs. In the treatment for cancer, biologics or biosimilars are used only as a secondary option where the patient does not respond to chemical treatments. "The products we target are very efficient and show limited side effects but, despite their existence, it is a shame that not every patient can reach them," said Deniz Demir, general manager of Dem İlaç, a company that is the first biosimilar licence owner and currently investing in a bio-manufacturing site for the development of monoclonals.

Because they are large molecules, biosimilars cannot travel everywhere into the body and are thus more targeted towards a specific location; this reduces the toxicity experienced in the case of a highly dispersible chemical drug. Nevertheless, biosimilars are yet to revolutionize access to treatment, mainly because there are barriers to approving these molecules. Guidance on biosimilars around the world is still considered vague in terms of establishing "high similarity" or "no clinically meaningful differences," the key correlative attributes that legitimize a biosimilar's use. Pursuant to the United States' Public Health Service Act (PHS), biosimilarity is described as "high similarity to a reference product notwithstanding minor differences in clinically inactive components," and no "meaningful differences" in terms of safety, purity and potency. The European Medicines Agency (EMA), the drugs regulatory body of the EU, has a similar definition. The evaluation of these criteria occurs through a rigorous stepwise approach, involving evidence to eliminate any uncertainty, starting from technology for characterization, animal studies for toxicity and comparative pharmacokinetic and pharmacodynamic studies, together with a clinical immunogenicity assessment and even head-to-head clinical studies from Phase 1 to Phase 4.

Murat Barlas, chairman of Liba İlaç and also President of the Turkish Biopharmaceuticals Platform (TBP), believes regulation in biosimilars needs to be better tailored to Turkey to reduce some of the bottlenecks facing clinical trials by using advanced analytical tools to prove bioequivalence: "Turkey needs to develop its regulatory affairs first. We cannot just copy the United States' FDA or Europe's EMA. The upcoming projects in biosimilars and biobetters are very interesting with huge investments. However, the biggest challenge for all these companies is that they get less time to market," he said.

Skipping some of the clinical steps to prove equivalence is an issue addressed outside of Turkey's context too. This is referred to as "Abbreviated licensing pathway," a legal recognition based on the assumption that the "copy" drug has the same efficacy and safety as the original and therefore the clinical development programme can be reduced. Clinicians and patients expressed their hesitance that biologicals are not as verifiable as chemically synthetized drugs; produced in living organisms and thus showing intrinsic variability, or micro-heterogeneity, there are no two identical biologicals, and the manufacturing conditions influence their quality. Thus, a "highly" similar rather than identical paradigm is applied. Dr. Gizem Dinler, associate professor at Istanbul Technical University (ITU), is confident in the power of analytical tools to prove bioequivalence: "It is vital for pharmaceutical companies to have good biophysical infrastructure to pass through the preclinical work."

Gizem's department obtained a government grant to buy the sophisticated instruments for structural biology.

In the EU the regulatory pathway to approve biosimilars was established in 2003 and, by November 2018, 50 biosimilars were authorized. Biosimilars market penetration in the EU is better than in the rest of the world, but substitution policies are dependent on each member state. For instance, in Spain hospital tenders do not allow biosimilars except for naïve patients (a patient who has never undergone treatment for the illness targeted by the experimental drug), while the Nordic countries accept full interchangeability at pharmaceutical level. Full interchangeability is the ultimate step in granting biosimilars recognition as an equal substitute to biologics.

As healthcare costs increase, developed economies like Europe, the United States, Japan Canada and South Korea are increasingly looking at biosimilars, but the way these jurisdictions adopt biosimilars will have an impact on the acceptance of these drugs worldwide. Differences in the regulatory pathway across countries can be an obstacle for biosimilar development in coming years, but global harmonization is likely to occur as in the case of generics. One way that these obstacles are tackled is through biobetters, or biosimilars that are not mere copies of the innovator, but which bring improved characteristics, be it improved stability or a more patient-friendly mode of administration. For instance, the first generation of biological, such as human insulin or the early versions of human growth hormone, are immediate release drugs administered through infusion or subcutaneously, but biobetters of these molecules use glycol-engineering to reduce the risk of immunogenicity, which makes the drug safer and requires lower doses, with a prolonged effect on the target. ■

Image courtesy of TÜBİTAK

Prof. Dr. Berrin Erdag

Chief Senior Researcher
TÜBİTAK MAM GENETIC ENGINEERING AND BIOTECHNOLOGY INSTITUTE (GEBI)

Could you provide a brief introduction to the institute and an overview of its development?
TÜBİTAK MAM GEBI is the national research institute for finding and conducting biopharmaceutical research and development in Turkey. Our institute has been working on the development and production of antibodies since 1992 for the diagnostics and therapy of certain diseases. We produce not only for Turkey but also for the global markets, therefore we aim to conform to international standards in terms of our infrastructure and personnel training. While numerous companies and institutions began their work with biosimilars, we chose to focus on developing original recombinant whole and partial monoclonal antibodies using antibody engineering. Our target is to develop valuable endogenous molecules with patent protection. We have several original novel recombinant anti-angiogenic monoclonal antibodies and peptide structures protected by patents from several countries such as USA, China, Korea and Turkey as novel reference drug candidates. We collaborate with national pharmaceutical companies to produce biosimilars as well. Although we have patents, commercializing novel original active molecules is not so simple. We rely on public funding and require solid grounds and collaboration with pharmaceutical companies to commence our projects.

Why is biotechnology an important sector for Turkey and what is your role in achieving milestones within this sector?
We believe that in the future, 30 out of the 50 best-selling molecules will be biopharmaceutical. The Turkish market has reached approximately USD 7 billion and 20% of prescription sales come from biopharmaceutical products produced locally and from imports. Seeing this opportunity in biopharmaceuticals, we want to seize the opportunity and learn the cloning of recombinant antibodies to produce microbiological entities and continue working on large antibody molecules that are approximately 150 kilodaltons. We have state of art equipment and experience in development, selection and production of the recombinant cells to produce biosimilars and original molecules.

How can the synergy between government, academia and the industry be improved?
Government has announced medical biotechnology is a priority technology area for funding. Soon after government started providing budget to institutions and private companies, which has contributed greatly to the development of biotechnology in universities, research centers, TÜBİTAK institutions and pharmaceutical companies.

What are the current research capabilities at GEBI?
Our infrastructure consists of nine laboratories and is key to the production of biosimilars and original molecules. Our patented anti-vascular endothelial growth factor (anti-VEGF) and anti-VEGFR2 molecules, peptides and monoclonal antibody fragments are now getting close to the market and this is something we have been studying for the past 16 years since 2003 at TÜBİTAK. Our aim is to work on therapeutically important recombinant antibodies and peptide structures for the future. We are establishing a new biotechnology center 'MEDIBIYO' where we will work on development of novel Mabs and Mab fragments as well as other novel diagnostic and therapeutic peptides for the health industry.
In addition to our strength in antibody discovery and production, we are expanding our research in various fields including theranostics (both diagnostic and therapeutic) and nanoparticle-based drug delivery for cancer therapy and diagnosis. In the application of theranostics photodynamic therapy, we are also dealing with developing effective compounds as a combination of highly competitive and effective new molecules which are anti-angiogenic and effective photosensitizer. On the other hand, nanoparticle based therapies and drug delivery system for anti-cancer agents especially functionalized with monoclonal antibodies (Mabs) are our new expanded field. Advances in recombinant DNA technology are the keys to pharmacogenomics and personalized medicine. These developments promise to result in more effective, individualized therapy and advances in preventive medicine. In this context, we will continue to work on a new generation of therapeutic approaches based on recombinant DNA technology.
We believe that the biopharmaceutical industry will have a strong impact on Turkish economy in the future and be placed among the first three industries strengthen the country's economic power. ■

Dr. Gizem Dinler

Associate Professor
ISTANBUL TECHNICAL UNIVERSITY (ITU)

We work on developing biosimilars in collaboration with some of the industry leaders. We obtained a large grant in 2016 that enabled us to pursue downstream development in ITU and buy state-of-the-art instruments for analytics that we provide as a service to the industry.

Could you briefly introduce your work?
Together with the MOH, we established a lab called "Genomic Lab", where we work on next generation sequencing for the development of personalized therapies. We also have a laboratory at a hospital, which lends us access to patients and samples for our genomic sequencing, thus enabling us to diagnose patients with mutations or genome-related diseases. We also conduct research with breast and colon cancer patients to deduce genetic variations specific to the Turkish population to help us develop personalized therapies for such patients. We have access to sizable grants in collaboration with medical doctors, and our students have the chance to work at the hospital as well. Another branch of my research involves drug targeting for certain protein interactions in cancer therapy. This is a fruitful part of the laboratory that helps us find therapeutic targets and we have released several publications on our related research.
Additionally, we work on developing biosimilars in collaboration with some of the industry leaders. We obtained a large grant in 2016 that enabled us to pursue downstream development in ITU and buy state-of-the-art instruments for analytics that we provide as a service to the industry.

What are the next generation medicines that the industry can expect based on your research?
While this is a complicated question to answer, the next generation medicines will depend on money because I believe the more you put in, the more you get out of your research. Most of the Turkish companies within the biosimilars space are trying to develop their own biosimilars, however, they realized that it is not easy without dedicating a large chunk of funds. These companies are waiting on decisions by the Ministry of Health in order to carry on with investments because at the moment, they are not feeling at ease. The Government is helping the industry by providing grants to kickstart research in biosimilars.

Could you comment on the preparedness of students and graduates to tackle such a knowledge-intensive field?
The students trained in my laboratory are recruited by companies such as Nobel and Turgut. Our aim is to train students and prepare them sufficiently for a career in the industry.

How cohesively do academic institutions and the industry work together in Turkey?
The industry is in the early stages of seeing collaborations between universities and companies. We work well with pharmaceutical companies because they are willing to help us and we in turn help them, leading to a mutually beneficial relationship with the common goal of achieving success. However, this is not commonplace and we hope that other universities will follow our lead.

What is the state of the infrastructure in university laboratories within academic institutions across Turkey?
In terms of biologics, pharmaceutical companies find it vital to have good biophysical infrastructure. The more sophisticated the instruments, the better the analytics, which allows companies to pass through a lot of pre-clinical work because you no longer need to prove certain things. For biosimilars, the EMA allows companies to prove their work by using these techniques and we need this confidence in our way of developing products for the quality of drugs and for the patients' benefit. We are pleased to have obtained the grant that allowed us to buy sophisticated instruments for structural biology, thus enabling us to conduct niche analyses through such projects.

Do you have a final message for our readership?
Pharmaceutical companies need to develop their own products rather than simply following the fill-and-finish method. Turkey needs more national products for our country and global players can contribute to this as well. Science should be heavily involved in the process and there are few companies that are taking this very seriously. ■

Hüseyin Yılmaz & Ece Öztürk

HY: MD, General Manager
EO: DVM, MSc. Business Strategy Consultant
HASBIOTECH İLAÇ

HY

EO

Can you give an overview of how Hasbiotech has evolved over the years?
Hasbiotech was established in 2009 with a very ambitious vision to become a pioneer in the biotech space. The company falls under the umbrella of the DEMIRYAKA HOLDING.
We have set our target on creating an original Turkish medicine which will be manufactured at our site, and we are also working to establish a manufacturing site for bringing the technical know-how to Turkey for manufacturing of biotechnological products and export of these novel medicines to the global market.

Can you give insights into Hasbiotech's product portfolio and capabilities in the biotech space?
We have a blockbuster product which has been in the Turkish market since 2012. HEBERPROT-P contains human epidermal growth factor which is produced by recombinant DNA technology. When directly injected into the wound, this growth factor ensures healing of deep and serious diabetic foot ulcers that are induced by diabetes and may usually lead to amputation of the foot.
It has gained an important place among the treatments of diabetic foot ulcers and those addressing the prevention of diabetes-induced foot amputation. HEBERPROT-P provides a fast, safe and effective wound healing process and has significantly reduced the rates of foot amputation caused by diabetes-induced foot ulcers in 26 countries where the product is already registered. We are also currently working on a new product assumed to be life saver and reducer of the complications of stroke.
Our areas of focus in the biotech area are focused on the needs in the market. We are in the process of constructing a manufacturing site where we will be establishing systems that will enable us to carry out contract manufacturing activities in accordance with good manufacturing practices and controls. Having manufacturing capabilities in Turkey will reposition our company in the sector. We are open for in-licencing and contract manufacturing cooperation. We are open to design our modular manufacturing site according to the needs of the clients.

Cuba was a primary focus and a starting point for Hasbiotech. Could you elaborate on how has this focus manifested?
Cuba, after the revolution, created a structure to develop its own medicines and improving the health system within the scope of socialist thoughts. By the accumulation of 50 years of knowledge, Cuba experienced a biotech boom which also started to be recognized by USA and European countries. The first boom was with an innovative medicine called Heberprot-P, which is also our blockbuster in Turkish market. Up to now, approximately 6,000 patients used Heberprot-P and, according to a retrospective study; the success rate is almost 90%.
By the innovative perspective gained and improved during all negotiations with Cuban institutes and scientist, HASBIOTECH decided to collaborate with Cuba for the development of a promising life saving medicine targeted to be used in heart attack. HASBIOTECH is the global partner of this medicine and responsible for the development plan.

What are Hasbiotech's objectives and vision for the next five years?
The entire DEMIRYAKA HOLDING has the aim to expand the know-how within the medicine area. We are collaborating with Cuba to enable the transfer of knowledge and technological advances. We want to foster and encourage innovation within the medicine sector in Turkey. Hasbiotech is very open for collaboration on biotechnology products and our aim is to build a healthier future by entering into a cooperative development stage on biotech products which will also lead us into a lucrative business model. In our search for innovative treatment options to be brought to use both in Turkey and abroad, we wish to establish long business collaborations and joint studies (in-licensing, out-licensing and co-development). ■

Deniz Demir, Ahmet Kuskonmaz & Esra Ustunyagiz

DD

DD: Chairman
AK: Exports Manager
EU: Head of R&D
DEM İLAÇ

Could you highlight some recent milestones?
DD: Dem İlaç is active in specific therapeutic agents, focusing on niche haematology and oncology products, mainly originals or what we call super generics (or high-tech generics). We are also the market leader in plasma derivatives, and the first Turkish biosimilars license owner. The past five years have set our company on a very fast growth path, which has made us one of the fastest growing companies in Turkey, according to IMS rankings. In this stretch of time, our priorities have been mainly in R&D and increasing our exports business. Through our sister company, Pharmada Pharmaceuticals, we concentrate on hospital products, the majority of which are dossier developments in injectable generics.
Turning to our latest developments, Dem İlaç has invested in a sterile manufacturing site and bio-manufacturing site, started in early 2013 and now reaching its final stages of completion. This site will cover an area of 12,500 square meters, of which 2,500 square meters are dedicated to biotech, especially to the development of monoclonals. The facility will run a nanotech manufacturing line in our sterile filling area, as well as a vials filling line, lyophilisation, and ampoule filling line, together with an extension project for pre-filled syringes.

What has encouraged Dem İlaç to make these investments?
DD: Low competition and high profitability in this field motivated us; however, the main driver for Dem İlaç is to bring valuable technologies to the country, and to make treatments reachable for all patients who are in need.

What is your take on the benefits and disadvantages that the localisation policy brings?
DD: The localisation project is a badly applied good idea. The MOH should be more lenient if the goals of the localisation policy are to be accomplished without it being seen to be too autocratic. The localisation policy should be carried out in a way that speaks positively of Turkey, and makes the country more attractive for investors and multinationals alike.

As one of the fastest growing companies in Turkey, what do you identify as the main pillars of growth in this evolution and how do you differentiate the company in an ever more crowded space?
DD: We never focused on the "easy" products, but instead, we have chosen the longer way to patents, selecting products which are difficult to register and to market. In this area, we have encountered less competition. Competition in the simple generics can be fierce and many generic companies are actually just rounding the wheel, while new entrants may not survive for a long time.

Dam Ilac has placed heavy emphasis on R&D. Could you tell us what are some of the key areas of focus in Dem İlaç's labs?
EU: Our main vision is to improve new technologies and build the know-how about biosimilars and nano-similars. We are working on three different areas- biotechnology, nanotechnology and peptide use. We are trying to develop our own cell-line and own media for scale-up technology. After completing our two biosimilars based on monoclonal antibodies, together with our nano-similar product which we hope to roll out, the next endeavour will be to work on original therapies. Throughout this process, we also act as an educational body by training our R&D staff to take a role in our team.

Which export markets are you concentrating on?
AK: Dem İlaç established its exports department five years ago and today we are working with more than 30 countries. Initially, we were focused on the MENA region, but this was not enough, and today our focus drifted to the regulated markets. To maintain an apt exports strategy, we need to monitor the political situation in each country- in a market like Libya, the strategy is devised in accordance to new developments, day by day. This is a crucial reason why regulated markets like Europe and America are preferred.
DD: The Turkish market is not our main focus. In every step of our strategy, we have always created very well developed dossiers, following the most reputable guidelines worldwide. In our future growth, exports play the biggest role. Even though we have a small number of products in our portfolio, we aim to make these globally available. ■

BRINGING IT ALL TOGETHER

» The biggest challenge for Turkey is the short-term thinking and lack of investment at a macro level; without commitments for long-term investments by the private sector, it will be hard to introduce novel products to the market «

- Prof. Dr. Mehmet Öztürk,
Director,
Izmir Biomedicine and Genome Center (IBG)

Image courtesy of Centurion Pharma

Bringing All Actors Together: Industry, University, Investors

THE TWO-WAY BRIDGE TO THE KNOWLEDGE GAP

Pharma and biopharma are much more distant relatives than their shared prefix may suggest. Biologics or biosimilars, which are larger proteins, peptides, nucleic acids or cells, pose different challenges in the development, production, commercialization and scale-up. Due to their larger weight, methods of preparation, route of administration, shelf-life, dosing, reactivity and other pharmacology considerations, pharma and biopharma are estranged in terms of the stages of drug discovery and development especially as far as cycle time, costs and risks or likelihood of success are concerned. Unlike chemical molecules with defined structures, large molecules have unique structures that cannot be replicated with exactitude, thus consistency is challenging for manufacturers who need to monitor the process more closely.

Based on these differences, biopharma is treated separately to classical pharma and it requires a different expertise. For these reasons, the biopharma segment is, by broad considerations, new to Turkey. The lack of industrial know-how in terms of biosynthesis and successfully completing compatibility studies will be a key issue affecting Turkish biopharma. Pharmaceutical companies entering this field need to train or attract new personnel with the adequate knowledge to work on an industrial scale, but this has not proven easy: "It is very difficult to find people with extensive knowledge and expertise in biotechnology in Turkey. The main reason is that there are only a few companies in this area which are actively producing biotech products," said Hakan Koçak, CEO of Koçak Pharma.

Even though universities are training students in the science of the latest generations of treatments, they can only prepare students to a certain limit. "While educational institutions contribute to basic scientific research, they do not provide industrial experience to students and their training does not fulfill the industry's needs," said Dr. Serdar Alpan, managing director of Turgut İlaç.

The initial governmental funds to incentivize biotech have helped to construct the hardware of the industry buying machinery, setting up the labs and igniting business in that space. However the software, including the R&D component, technical expertise and the capabilities of employees are even more important to address.

Over half of the students working in pharma are educated to degree-level, by nature of the highly knowledge-intensive field. The government set up 32 Biotech and Research Parks in the 1990s to create platforms for universities, research institutes and the industry itself to exchange technology. New educational courses are more tailored to the latest developments and the needs of the sector. At private university Acibadem a new course in microbiology was started three years ago, the first cohort including 71 students. With money from both Turkish government institution Tübitak, as well as funds from the European Council, the tuition fees, normally reaching up to US$10,000, were scraped for most students: "We wanted to make sure we select the best students and expose them not only to traditional classes, but also experience in empirical research projects," said Professor Tanıl Kocagöz, who is head of the Medical Microbiology and Biotechnology departments.

However, the fabric of a solid knowledge base is sewed from both theory and practice, and it involves academia as much as it involves industry. Besides funding pharma companies, grants offered to the industrial players were matched by grants to universities to develop their competence in this field. Istanbul Technical University (ITU), one of the oldest universities in Turkey, established a "Genomic Lab" with funds from the MoH to work on the next generation of sequencing for the development of personalized therapies. Scientists at ITU conduct research with breast and colon cancer patients. In 2010, the government also made a state call for the establishment of research centres. Sunum, which stands for Nanotechnology Research and Application Centre, received a US$35 million investment from the Ministry of Development. Over time, Sunum also created its own financing streams through industrial partnerships, becoming semi-autonomous. These centers are thought to bridge the gap between the remote academia and profit-focused industry.

Funds addressed to both industrial players and academic research centres, especially in the development of biosimilars, have facilitated collaborations between the industry and academia. Tübitak's 1004 project stands out as one of the programs that brought these two loose ends together. Atabay, one of the well-established pharmaceuticals company and a leader in paracetamol production, is a forerunner in university partnerships, with eight collaborations in total. Since 2015, the company has worked with ITU and Marmara University's Department of Pharmaceutical Biotechnology to produce a biosimilar product starting from cell bank to final product, completing the know-how arch and removing the need to import proteins. 23 scientists were also thus trained at Atabay.

Doğan Taşkent, board member of Atabay, is also on the board of the University Industry Collaboration Centers Platform (ÜSİMP) and an authority on what these collaborations entail: "We noticed that in Turkey the collaborations are not between the university and the industry, but are tied between an academician and the industry. We need to change the nature of this contract from the individual to the institution," he said.

Because of the legal framework, the responsibility is shifted away from the university body to the individual professor, which does not make universities accountable or reliable in long-term projects that can last up to 10 years.

When Turkish Prof Tanıl Kocagöz returned from his studies at the University of California in 1994, he wanted to convince his country's academia of the importance of industry-university collaborations: "It became clear to me that the success of American biopharma was due to this prolific collaboration; the headquarters of the largest biotech companies are located near the campuses of universities like Stanford," he said.

It took another decade before Turkey realized the importance of this key partnership. Now, Professor Tanıl Kocagöz is head of Departments of Medical Microbiology and Biotechnology at Acibadem University where he has been able to realize his hopes. Three years ago, he started a partnership with Turgut İlaç to produce biosimilars. Although he does not deny the importance of biosimilars in bringing money into the country, his hopes go further: "Without producing original products, our survival will be limited to imitating others. Of course we can start with producing biosimilars, but this should not be the end point in sight." ■

Collaboration Between Industry and Academia

Prof. Dr. Ercument KARASULU
EGE UNIVERSITY RESEARCH AND APPLICATION CENTER OF DRUG DEVELOPMENT AND PHARMOCOKINETICS (ARGEFAR)

One of the most important goals of modern education is to train undergraduates and graduates practically in the related field. This issue is very important especially in new and innovative areas. The most important step to be taken to solve this is for the last year of undergraduate education to take place in the industry, or for the industry to take an active role in education in certain periods in postgraduate education. For this purpose, universities, institutes or research and application centers that provide education, especially in the field of biotechnology, are the most important units for cooperation with industry. Not only the staff with academic training, but also researchers who want to receive academic training from industry, can thus have an important opportunity. Tübitak's doctoral-industrial projects and Higher Education Institution (YÖK) 100/2000 YÖK PhD Scholarship are the most vivid example of this.

Ege University Research and Application Center of Drug Development and Pharmocokinetics (ARGEFAR), which carries out almost all stages of the pre-clinical and clinical research processes of reference biotechnological/biosimilar and synthetic drug molecules in our country, has raised many researchers with postgraduate education and directed them to industry or accepted researchers from industry with their projects for postgraduate education. With the involvement of clinicians in this process, translational researches carried out, especially in the biotechnology field, will be an important opportunity for our country and the world. The deficiencies and requirements that clinicians have experienced and identified in the field have reached a point that can only be solved by the collaboration of both academicians and industry.

The main purpose of our center is to pave the way for research in this direction by using translational research with chemistry, biology, biochemistry, pharmacy and medical sciences. We encourage our employees working in our center to receive postgraduate education in order to train them in the relevant field. We organize their working hours in accordance with their education schedules and provide flexibility to our employees. At the same time, by bringing the researchers in our center together with industry representatives, we enable them to better understand the needs of the industry as well as enabling them to reach the competence needed by the industry. Providing "learning by living" at higher education, as in our center, will have an important contribution in bringing the competent graduates needed into the business life.

If such a strategy is followed, our country will be a stakeholder in these developments and even be able to lead important matters in the process, instead of following the point the world has reached in the biotechnological field. ■

Zeynep Atabay Taşkent & Doğan Taşkent

ZAT

DT

ZAT: Owner
DT: Board Member
ATABAY

Please update us on the most recent developments taking place in the company?
Since 2015, we have been running the biotech project supported by TÜBİTAK to produce a biosimilar product, starting from a cell bank all the way to delivering the final product. This project is being conducted in collaboration with two universities: ITU's Molecular Biotechnology and Genetics Research Centre, and Marmara University's Department of Bioengineering. Bioprocess and OMICs Engineering Research Group are also part of the collaboration and the project is also receiving government support. This triangle of partnerships works very well. We have just completed our pilot production and are now starting the pre-clinical stage. We create almost everything, from downstream to upstream processes and analytics. Atabay has the first GMP-certified master cell bank produced in Turkey, and our R&D centre has received the official certification of the Turkish government. This year we are also expanding into herbal-based medicines, which marks a new focus for the company.

Could you elaborate on the symbiosis between the company and public and academic stakeholders?
The master cell bank we are assiduously working on is not simply a commercial project, but also a knowledge building project. Three other companies (Ilko, Deva and Nobel) received grants from the government, and we are all working together (biosimilar pre-clinic and clinic studies' policies, financial support mechanisms and standardization of processes) in a way that creates an ecosystem.

With the objective of creating these knowledge chains between the scientific world and industry, how could university-industry collaborations be further fostered in Turkey?
We've noticed that in Turkey, the collaborations are not between universities and industry, but are between an individual academic and industry. We need to change the nature of these contracts from individual arrangements to institutional ones.

Atabay stands out as one of the few APIs producers in the country. What are the advantages of continuing this line of production?
Atabay is one of the few Turkish API producers, with half of our API production going into captive consumption for our own formulations, and the other half being sold in export markets. There is a strategic advantage in this, both for the company and for Turkey more broadly. We produce paracetamol and oseltamivir phosphate APIs for influenza. Whenever there is an influenza outbreak, it becomes very difficult to source the APIs because the producers sell mostly to big pharma, with the rest waiting in line.
Another advantage is that it allows us to control the pricing, which is crucial when you consider the fluctuations of the Turkish lira against the dollar and the euro.

What is your experience of commercialising Turkish products on global markets?
Since 1985, Atabay has received GMP and FDA approvals for APIs, and we are selling APIs around the world. We have been selling finished dosage forms mainly in our region. With the recent EU GMP facility, which includes production for sterile products, we are targeting the EU market. All Turkish pharma companies want to export and it is important to create regional hubs such as a "Pharma Valley Turkey" to gain recognition for quality and reliability.

Could you share your vision of how Atabay may develop in the future?
At Atabay, we are selling 50 million packages of paracetamol yearly, at very reasonable prices, and reaching the homes of everyone who needs the medicine. Not many pharmaceutical companies will enter this low-margin market. But for us, two things flow from this reality: first, we are driven by the desire to have an impact on the population, to assume responsibility for reaching the people in the streets, and to be a company with a purpose.
Second, we would like to create enduring brands backed by APIs, to guarantee the supply of medicines, independent of the vagaries of the world economy or world politics. Last year, when the euro went up, and pharma companies stopped importing medicines, we continued production despite the losses incurred, in order to guarantee hospitals an uninterrupted supply. Our employees, shareholders and various stakeholders together play a role in making Atabay a company with a social mission, which we hope to carry on to the fourth generation and beyond. ■

Prof. Dr. Tanıl Kocagöz

Head of Departments of Medical Microbiology and Biotechnology
ACIBADEM UNIVERSITY RESEARCH LABORATORY

Acibadem University is a private university founded in 2007, belonging to the Acibadem Healthcare Group. Professor Dr. Kocagöz is a microbiology and infectious disease specialist.

Since joining Acibadem University 10 years ago, one of your priorities has been to nurture university-industry partnerships. What progress has been made in this regard?
Since my time in the US, it became clear to me that the success of American biopharma was due to the prolific industry-university collaborations. The headquarters of the largest companies are located in the campuses of universities like Stanford; when a product is developed in the research labs, it is launched into the market, and a share of the profits are reinvested in research, which speeds developments by creating an innovation cycle. Returning to Turkey in 1994, I sought to convince people in the academia of this model, but it took over a decade before the importance of industry-university collaboration was brought into focus. Similarly, Turkey also realised the importance of biotech very late, but there is still a chance to catch up, with collaborations starting to form. Concrete relations, however, have only started to materialise in the past few years.

You also have experience as an entrepreneur, having founded TIBO in 2005. Could you share more details about TIBO?
We founded TIBO, which stands for "Trends in Innovative Biotech Organisation" in 2005, focusing first on developing diagnostics, which are easier and cheaper to develop compared to therapeutic drugs. Using microbials to introduce diagnosis, the costs are minimal because human studies do not need to be carried out. TIBO is specialised in rapid diagnosis for infectious diseases, with a focus on tuberculosis (TB). I developed a sample processing kit together with a rapid tuberculosis culture system. These products were brought to the attention of WHO because they are simple tools with great usability in resource limited settings where TB continues to take many lives. Without the resources for diagnosis, one third of people who die of TB are never diagnosed. WHO has set out to reduce the number of fatalities by 90% by 2030, and fully eradicate the disease by 2050. There is great scope in this area, but so far we have not been able to launch these products internationally. While TIBO makes US$400,000 worth of product in a year, global competitors produce about US$4 billion equivalent in the same amount of time. It is my dream that the company will manage to establish an international collaboration to do global marketing and face competition better.

The biotech industry is still in its early stages. What potential does Turkey have for developing original drugs?
First of all, we have to trust ourselves, and fight against the belief that developing drugs is too expensive, because this is only partly true and should not discourage our attempts. At this stage, research centres are able to conduct the first part of the research up to bringing the final product to the market, from lab studies, animal testing, and even Phase 1 Clinical studies, with the financial help of research organisations like TÜBİTAK and TUSEB. In the universities, there are many drugs under discovery of which the industry is not even aware. On the other hand, in the industry, even big companies who hire over 150 scientists in their R&D teams do not engage in research that will lead to an original drug with a prominent effect. These two components need to be brought under the same roof.

What is your message for our international audience?
There is a misconception that nothing innovative can come out of an industrial country like Turkey, that the research and ideas here are not developed enough to bring original research products. This is not true. We have very educated young talent and we need to organise these assets and bring together the universities and the industrial players, not only from Turkey, but at an international level too. Investors and international companies should come and look at what is going on in Turkey because what we are doing is not only for our country, but for humanity. ■

Prof. Dr. R. Serdar Alpan

Head of Biotechnology Group
TURGUT İLAÇLARI (BIOPHARMACEUTICALS)

Could you provide a brief introduction to Turgut and highlight some recent milestones?
Turgut Pharmaceuticals was founded in 1959 under the name of Fako Pharmaceuticals and became one of the leading pharmaceutical companies in Turkey within 10 years of its inception. Kaya Turgut, the founder, grew the company by establishing long-term global collaborations with big pharmaceutical partners. He not only sold these companies' products but also brought their technology to Turkey, thus becoming a pioneer of new investments, such as the first penicillin API production in the Turkish pharmaceutical industry. Fako Pharmaceuticals had successfully attained approvals in Europe and the United States and exported to these highly regulated markets. In 2004, Fako Pharmaceuticals sold the generic business to Actavis and quit the commercial business. I met Kaya Turgut in late 2013 and together we established Turgut Biotechnology Group in January 2014 and made one of the largest biotechnology investments in Turkey. Today, we have 50 employees working in Turgut Biotechnology Group.

What are the present gaps in the market for biotechnology and biosimilars and how can Turgut help fill that gap?
Our strategy was focused on a biotechnology platform including cell line development, process development, protein characterization, process scale up and large scale GMP production. In addition, we carefully selected and invested in young scientists and created the first generation of Turkish biotechnology experts. We established strategic partnerships with selected expert companies and transferred advanced industrial technologies and this strategy has enabled us to establish our own biotechnology platform. This biotechnology platform ranges from industrial cell line development to large scale production with all the steps in between. We also established a successful industry-university collaboration where we have a fully owned R&D center that is managed by us on the university campus. We have also built a GMP production facility on the outskirts of Istanbul in the Gebze Organized Industrial Zone that will open next year.

What is Turgut's focus in terms of the products it develops?
We develop and manufacture our own biosimilar monoclonal antibody products to the standards of Turkish MOH, the FDA and the EMA. For this purpose, we established an R&D based biotechnology platform for the development and manufacture of high quality biosimilar monoclonal antibodies. These products have already achieved immense success globally in terms of sales and their patents have recently expired. On our biotechnology platform, we developed five industrial cell lines expressing five monoclonal antibodies and three small scale process developments, of which two are GMP productions and one is in the clinical trial phase. Turgut's investment is in the monoclonal antibody APIs that are very successful in changing the landscape of various therapeutic fields. Our aim is to produce these APIs within Turkey and increase the access of these drugs in Turkey and global regulated markets. We will continue to invest in R&D and people for sustainable growth.

How could companies such as Turgut and Universities mutually benefit from strategic partnerships?
While educational institutions contribute to basic scientific research and develop new technologies, they do not, naturally, have industrial experience. Universities and industry complement each other when they collaborate and successful industrial products can be developed as a result. In terms of providing a smooth transition into the workforce for students, most companies within the industry have a training system to onboard students and other employees.

Do you have a final message for our readership?
Big pharmaceutical companies create value through R&D and we would like to prove this principle within the Turkish industry through our R&D-based biotechnology platform. Importing APIs and providing the fill & finish locally is only contributing to a fraction of the entire process, however producing the API locally means creating the majority of the value. Our biotechnology platform is key to succeeding in biotechnology within Turkey and, we believe, we will prove that R&D investment creates value in the Turkish pharmaceutical industry and encourages investors to bring more money into the field. ■

INDUSTRY VIEWS ON BRIDGING THE KNOWLEDGE GAP

"To add true value to the Turkish pharma industry, we need to get into R&D sooner or later, because innovation is the only way we can obtain meaningful profits to the country."

- Mehmet Goker, CEO, TR Pharm

"We need to take a step back before rushing into biologicals: first, we need to fully consider R&D, starting with the R, and then the D, before the B of biologics. For this, the government needs to look into legislation to bring universities on board and create a three-legged support between the government, universities, and the pharma industry."

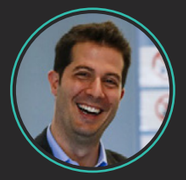
- Faik Somer, CEO, Birgi Mefar İlaç

"Most Turkish companies within the biosimilars space are waiting for decisions from the MoH to carry on with the investment because currently they are not feeling reassured the support given so far will be continued."

- Dr. Gizem Dinler, Associate Professor, ITU (Istanbul Technical University Molecular Biology-Biotechnology and Genetics Research Centre)

"What our scientists and engineers develop in the lab does not get translated into the industry, intercut by missing links in the sector. We need to bridge these two realms; the government is supporting some capital venture funds to invest in start-ups with a focus on high-tech platforms."

- Prof. Dr. Mehmet Öztürk, Director, Izmir Biomedicine and Genome Center (IBG)



"Were I asked today if I'd make the same investment in Turkey once again, the answer would be yes, but with the big contention that my firm should be ran from two offices- one in Europe and one in Turkey. Turkey is indisputably advantageous, but the market and the investors need to be reminded of these advantages."

- Cem Erdem, CEO and co-founder Florabio

"Even big companies with R&D teams of over 150 scientists do not engage in original research with a prominent effect. On the other hand, in the universities, there are many drugs under discovery that the industry is not even aware of. These two realms need to be brought under the same roof."

- Prof. Dr. Tanıl Kocagöz, Head of Department of Medical Microbiology and Biotechnology, Acibadem University

Aiming Further: The Long Way to Original Research

Image courtesy of IBG

Pharma players, for years conditioned by a mentality of rigorous cost saving, are partially reconfiguring their business models to one characterized more by spending than by profits, at least at an initial phase. Cinnagen, a company that has invested US$600 million in its pipeline, will spend between US$30 million to US$50 million on each biosimilar drug before it reaches the market. Stepping in with understandable caution, even large companies with big R&D centers often do not engage in original research that will lead to breakthroughs in the industry. As Hüseyin Yılmaz, general manager of Has Biotech, stated: "The Turkish market is more focused on the commercial space rather than the scientific space."

However, Professor Tanıl Kocagöz from Acibadem University believes that the obstacles can be overcome and points at the drug discoveries taking place behind the doors of universities and research centres: "First of all, we have to trust ourselves and fight against the belief that developing drugs is too expensive; secondly, we need to fight against the misconception that nothing innovative can come out of an industrial country like Turkey."

Developing original drugs is a risky business because the money put into development must also cover the costs for all failures, and these are likely to be numerous. High-attrition and high-costs are some of the most powerful factors in influencing behaviours in original drug development. Biotech production also changes the way manufacturers look at the purpose of the investment. In traditional pharma manufacturing is the primary focus, tagged to which R&D investment represented minor figures, but in biotech production, R&D costs make up to 70% of all investment.

Technically advanced work on both upstream and downstream processes as well as work in developing original molecules is confined to research centers that bridge the steep knowledge gap in biotech. GEBI-Genetic Engineering and Biotechnology Institute, belonging to Tübitak, is the national research institute for finding and conducting biopharmaceutical research and development in Turkey. This year is the 16th year of development for its original molecule, which is nearing market entry. In the fashion of American or South Korean PPPs (public-private partnerships), newly created research centers act as intermediate entities in the transfer of knowledge. These are able to carry out the initial stages of research and product development, from laboratory studies to animal testing and up to Phase 1 of clinical studies, mostly supported by public grants. Despite the government's investment, this research is often not turned into an output that can benefit society: "There is a problem in the seamless transformation of an idea to an end-product," believes Professor Fazilet Vardar Sukan, director of Sunum Research Centre.

There are many ideas simmering in the labs that do not reach the ears, interests or the pockets of industrial partners. For instance, Biomedicine and Genome Centre (IBG) is one of the few to engage in original molecules especially in the area of rare diseases and cancer treatment, collaborating with three American start-ups and one Turkish company for biosimilars development, but little of the original research sees the light out of the lab: "Without commitment for investment by the private sector it will be hard to introduce novel products to the market," said Mehmet Ozturk, director of IBG.

The government funding initiated a kick-start to the sector, but these incentives must be met by private investment, otherwise, many of the biotech projects are on stand-by. ■

Defining a Niche Market for Competitiveness of the Turkish Pharmaceutical Industries

Professor Fazilet Vardar Sukan
Director
SUNUM (SABANCI UNIVERSITY)

The Turkish pharmaceutical industry goes back to 1950's and has experienced many set backs since then. Investments of foreign capital companies into the Turkish pharmaceuticals market started to increase during the 90's. Currently, there are 70 companies active in pharma manufacturing, of which 14 are multinational manufacturing companies and 11 are raw material producing companies.

Turkey is well placed to act as a regional hub to supply finished formulations across the Eurasian continent covering CIS and MENA regions and the pharmaceutical production trends are closely related to domestic and foreign demand. According to 2019 statistics, the Turkish pharma market is ranked 17th within the global market, supplying more than 11,000 products. However, although exports have been increasing steadily, Turkey is still dependent on imported drugs, particularly for originator products. The originator drugs dominate pharma sales in terms of value with about 70%, and their share in unit sales is about 40%.

However, Turkey's dependency on imported pharmaceuticals is unsustainable, hence Turkey is prioritizing local production. According to 2018 statistics, R&D spending in the 31 R&D Centers of the pharmaceutical sector increased by 241% between 2010 and 2017. Current State policies encourage export substitution through the manufacturing of generic products. Local products in the market have increased by 158 % in value and 49 % in units, in the same time span.

Skilled labor force at a low cost, as well as strong public support for manufacturing and R&D through incentives and R&D funds, provide vast opportunities for the development of new products, and this has lead certain Turkish companies to initiate projects in recent years, primarily for developing new generic products.

However, there is now a wider acceptance that market entry needs to be based on more than just acquisitions and generics, as margins in this part of the market continue to decline. The future of the industry lies in niche products and, unless the Turkish pharmaceutical sector can develop these products, it will struggle locally and globally in the future.

Turkey, being in the temperate climate zone, possesses remarkable characteristics in terms of plant diversity. The number of plant species spreading throughout the country is close to the number of plant species within the European continent. It is known that there are nearly 12,000 plants in Turkey of which 35% are endemic, compared to 2,500 endemic species in Europe. Today, many plant-derived compounds are used in the pharmaceutical industry and plants are important sources for new lead compounds. However, although medicinal plants and endemic plant germplasms are extensively used worldwide to address a variety of health problems, there are major issues such as low yields, efficiencies and high costs.

On the other hand, nano and biotechnologies offer vast opportunities to exploit the structures and processes of biomolecules for novel medical applications creating the rapidly growing field of nanobiotechnology. While plant genetic resources can be utilized with a range of biotechnological methods, such as in vitro plant cell and organ cultures, micro-propagation techniques, application and exploitation of nanotechnologies facilitate interaction at sub-cellular/molecular levels of the body with a high degree of specificity. Nanotechnology involves manipulation of physical as well as chemical properties of materials at molecular levels. Biotechnology uses the knowledge and techniques of biology to manipulate molecular, genetic and cellular processes to develop products and services

Nanobiotechnology is considered to be the unique fusion of biotechnology and nanotechnology by which classical microtechnologies can be merged into a molecular biological approach opening a novel path for new drug development. The expense and time involved in traditional biomolecule design limit the availability of bioactive molecules. Nanoscale assembly and synthesis techniques provide an alternative to traditional methods.

Target molecules and atoms can be physically manipulated on solid substrates by attaching them onto bio-membranes and controlling where and when chemical reactions take place in a fast process that requires fewer materials (reagents and solutions). Thus, the ability to carry out chemical and biological reactions on solid substrates, rather than through the traditional solution based processes, is improved.

Nanobiotechnology can develop drugs for diseases that conventional pharmaceuticals cannot target, such as new drug formulations with less side effects and faster routes for drug delivery. It can enhance drug efficacy and reduce drug toxicity through selective localization and better cellular transmission and retention. New formulations can enable delivery to targeted sites, including locations that cannot easily be reached by standard drugs, exploiting the distinct patho-physiological features of diseased tissues.

Thus, Nanobiotechnologies open up vast opportunities for the pharmaceutical industries with novel applications, reducing drug discovery costs, providing a large diversity of compounds and facilitating the development of highly specific drugs. Turkey can create a niche for its pharma industries by exploiting its endemic plant species for isolation of novel biomolecules coupled by the scientific and technological expertise of its academia. The Turkish research community with its very potent and qualified skill set and infrastructure in nanobiotechnology is ready to make its contrition to the pharmaceutical sector if efficient pre-competitive research collaborations can be established supporting mega-projects nationwide. ■

The Investment Scene

Looking at other countries that have dramatically developed their biotech sector, South Korea comes to mind as one of the world's most innovative countries. The commitment of the Korean government to developing innovative sectors was coupled with strong initiatives in education, Korea being one of the biggest spenders on education in the Asia Pacific region. The government pours billions of dollars into the development of new drugs and supports venture firms and start-ups in biotech. Turkey's approach aims to emulate South Korea in turning biotech into an engine for the economy. To do so, the government needs to lend its full support: "Looking at countries like South Korea, Egypt, India or Argentina, one notices that the biotech sectors achieved success because the authorities conferred market protections. In Turkey, there are a number of biotechnology companies, but if we look at market shares, not one of them is in a strong position to grab higher takes," said Ersin Erfa, CEO of Centurion.

Start-ups supported by venture capital firms are the traditional commercial intermediaries to send an idea from paper to profits. However, Turkey does not have a strong start-up culture in biotech. The Turkish biopharma sector is mostly made up of the old companies exploring new ground, with a few start-ups scattered in the landscape. Often, the new entities are spin-offs of parent companies with stakes in classical pharma and other verticals. Arven, for instance, is the largest investment made by parent group Toksöz in a high-tech production facility of 28,000 square meters. Other start-ups likewise rely on personal and professional connections to fund their ideas. Gizem Dinler, associate professor at Istanbul Technical University, believes start-ups cannot be integrated in the ecosystem because large firms galvanize all investment sources: "These are the rules of the game, but the government should intervene to push for the industry to prosper as a whole," she said.

In seeking investment for Florabio, a start-up launched in 2016, founder Cem Erdem has been confronted with another challenge facing the wider sector. Explaining to investors Florabio's product – a cell line development bank – has proven to be one the most difficult aspects. The language of biotech is new and its mastering requires patience. Investors tend to be oriented towards tangible products with immediate results and the development of biopharma products is anything but short or easy to explain: "The investors that we approached did not know enough about biotechnology and we had to educate them about this industry to encourage their investment. There are some companies that are willing to invest in biotechnology, but these companies are looking for something tangible and are not necessarily confident to invest in a start-up company," explained Erdem.

Eventually, Erdem used US$3 million from personal savings and found a German bank interested to lend the rest. Three months after the company was founded, the coup attempt took place, driving inflation rates up and scaring investors off for the longer term. The Turkish banking sector, which is comprised of a stable number of 50 banks, became even more inaccessible for SMEs like Florabio. The consequences of the crisis of 2018 are still palpable on the investment side. The high interest rates make funding incredibly expensive, businesses dependent on foreign materials and imports ran into difficulties. With many companies going into debt or debt restructuring, private investments crashed. President Erdogan pleaded to bring both the bank rate and inflation under single digits. The national bank slashed the rate by 10% in the first manoeuvre referred as quantitative easing to pump cheaper money into the economy. Since July 2019, interest rates have been repeatedly cut from their peak in 2018 at 24% to rest now at 9.75%. Economists warn there is little room for further decrease given the risks that inflation may increase again.

In the past five years, credit extension to the private sector increased from 51.2% of GDP in 2013 to 63.6% of GDP in 2018, stalling in the second half of 2018. High levels of external debt is one of most the persistent challenges for Turkey's economy. The unpredictability of these cash flows, with debt expected to mature at the beginning of 2020, weans investor sentiment. Policy uncertainties have not been enticing foreign investment either, which today is at a low 1.7% of GDP. Bearing such risks in mind, financial institutions are less likely to offer long-term investment to SMEs as compared to larger corporations. To support businesses the government is offering measures such as providing credit instalments and incentivizing SMEs through financial aid. For instance, authorities launched a Credit Guarantee Fund to help of SMEs.

Unsurprisingly, the wider consequences of market instability are reflected in a reluctance to invest. At odds with the long gestation of biotech projects is a shortsighted investment culture. "Turkish investors are risk averse and unwilling to commit their capital for longer than three to five years. This mentality is not compatible with start-up culture, which requires 10 to 15 years to see a return on investment," explained Dr. Mehmet Öztürk, director of Izmir Biomedicine and Genome Center (IBG).

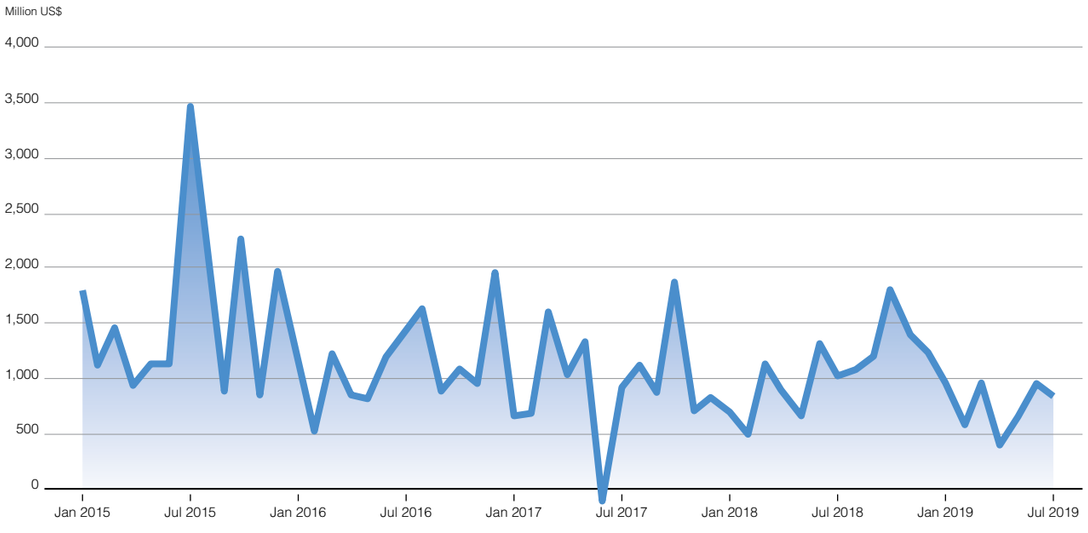
For Arven, a start-up and the recipient of a large investment made by its parent company, Toksöz, it took seven years to bring its DPI (Dry Powder Inhaler) device to the market. Before it can secure further investment, Arven has decided to become a CDMO, producing therapeutic proteins and offering services in similarity studies, bioassay studies or receptor binding studies. "In Turkey, one cannot predict the future further than tomorrow and thus it is difficult to make precise schedules with defined targets. The pharmaceuticals business is a challenging industry across the world, but it is 10 times more so in Turkey," said Deniz Demir, general manager of Dem Ilac.

Expectations are high in the next three years, but so is a feeling of uncertainty. The 11th National Development Plan, the broad policy manifesto through which the priorities of Vision 2023 are identified, targets the improvement of the business and investment climate as one of the 25 priority transformation programs. Turkey's 2023 Vision is premised on expansionary macroeconomic policies, including higher spending and incentives to bolster consumption, employment and investment, but the country's economic plans should also include efforts on increasing transparency and promoting savings rather than corporate indebtedness. Re-asserting macroeconomic credibility needs to be a prime consideration to avoid further capital flight and reduce risk.

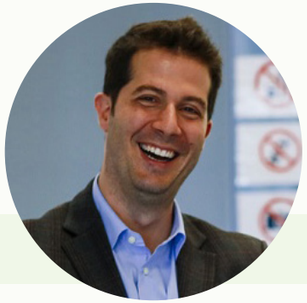
Turkey's chance to become a leading pharma production hub annotated on the world map is contingent on its ability to tie-in the different strategies on the axis of local production, global expansion and upgrading to high value products. Biopharmaceuticals need to pursue from the very beginning a global strategy to legitimize large investments. If this is successful, the trade deficit can not only be reduced, but also reversed. "All the elements are there," said Zeynep Atabay, owner of Atabay, referring to the technical and scientific acumen, the industry players and willingness on the side of the government, but she stresses: "These elements need to be orchestrated in a coordinated manner and the right capital invested in the right projects." ■

TURKEY'S FOREIGN DIRECT INVESTMENT

Source: CEICDATA, Central Bank of the Republic of Turkey



Cem Erdem



CEO and Co-Founder
FLORABIO TEKNOLOJI

Florabio is a life science company with proprietary technology, know-how and experience in research and development of therapeutic proteins.

Can you give an overview of Florabio?
Our business model was to create a company to support Turkey with a local supply of cell lines and media. Florabio's unique glycoengineering platform enables us to achieve extremely comparable biosimilar cell lines.
The second and the main business of Florabio is cell culture media development. If cell line is considered as the engine of a car, media can be described as the fuel for the engine to work. Florabio established one of the best media development platforms which enables us to develop any cell culture media in 4-6 media for any cell line including customer specific cell lines.
From the R&D perspective, we are ahead of our goals and strategies with the products we developed and commercialized. Florabio has four basal and five feed media for four different cell lines focusing on recombinant protein, vaccines and gene therapy applications. We have already licensed out one of our media developments to a global supplier. This has become the first and only biotech licensing that Turkey offers to Europe. The product will be marketed to 200 countries under the global supplier's name, but the IP will still belong to Florabio.
We are currently under negotiations for licensing out our other products.
At the same time, we finalized two cell line development projects which were supplied to the Turkish market serving as the first locally developed cell lines. Florabio is developing cell lines and medias for off the shelf purposes as well as for customer specific requirements.

What are the advantages of operating in Turkey?
High quality/cost effective labor and low cost operational advantages are the most important. Another important advantage is the government's intensive support for biotech R&D.
Besides all the advantages, we also have some disadvantages including rent and supply chain management of consumables and chemicals. For example, the rent cost at any technopark at one of the three big cities is almost double as much as the rent at the biggest cities of Germany.
The supply chain in Tukey is also a challenge, but if you have enough capital to stock inventory, this challenge can be overcome.

Is Florabio positioning itself to become a global supplier?
We already are an international supplier with our licensing agreement which enabled our products to be used in 200 different countries. In addition to our licensing agreements, we are about to sign distributor agreements with China and Korea. In less than three years time, our plan is to achieve minimum 3% market share which is not ambitious at all due to our platform technologies.
Either by utilizing the available capacities around the world or even investing in our own production facility, Florabio plans to be one of the top media development and supplier companies in the world in very short time.

How did Florabio raise capital to start the company?
It was challenging to acquire capital due to fact that Turkish investors were lacking knowledge on biotechnology. To date we have invested approximately 3 million Euros from our own pockets.
Unfortunately, three months after the company's establishment, there was a coup attempt in Turkey, which also stopped Government support activities and deterred investments.

Do you have a final message for our international readership?
Florabio is one of the top life science companies with proprietary technology, know-how and experience in manufacturing therapeutic proteins or antigens in the shortest time.
On the other hand, Turkey is a dynamic and ambitious country with a proven track record of success stories in the pharmaceutical sector. The level of experience, know-how and the quality of labor in Turkey is the key factor for such success stories. As the first and only biopharmaceutical R&D startup of Turkey, we decided to invest in Turkey because of all of these reasons. ■

Fatih Yedikardeş

General Manager
DAIICHI-SANKYO İLAÇ

Could you start with a brief overview of the company, highlighting its most recent milestones, and its position in the Turkish market?
Daiichi-Sankyo's mission is to contribute to the enrichment of the quality of life using innovative pharmaceuticals. As a global pharmaceutical company with origins in Japan, Daiichi-Sankyo is present in more than 20 countries, including Turkey since 2008. We are working to realize our 2025 vision of being a 'Global Pharma Innovator with a competitive advantage in oncology'. To that end, we are striving to satisfy a variety of unmet medical needs as a developer of new drugs, including vaccines, generic and OTC drugs. Our operation in Turkey is relatively young, yet we manufacture 90% of our products locally in cooperation with Abdi Ibrahim. Our aim is to make Turkey our regional hub in the mid-term.

What are Daiichi-Sankyo's core competencies and products?
Our competitive advantage is in oncology. As part of our 2025 vision, our second product was approved by the FDA in 2019. Lixiana is among our core products as an anticoagulant medicine that prevents strokes and systemic embolism in patients with non-valvular atrial fibrillation (irregular rapid contractions of the upper chambers of the heart).

Innovation being the DNA of the company, how do you balance costs in a high-risk environment with creating value through innovation?
Due to the high risk of our operations and the recent financial limitations to healthcare expenditure we invest in core markets such as Japan, US and the EU, in addition to some emerging/developing markets. Our wide portfolio of generics, vaccines and over-the-counter medicines allows us to adapt to our environments accordingly and balance risk. Hence, our 2025 vision captures this flexibility and innovation.

What is the significance of the localization policy in the long-run for the Turkish market and its implications for fair competition?
We believe that localization is an important initiative for local pharma industry producers and the country's economy due to the potential capacity of production. Today, 90 of every 100 boxes of Daiichi-Sankyo's products that reach patients in Turkey are manufactured in-country.
In order to ensure the sustainability of the localization process, it is important that global companies consult with the decision makers and cooperate to ensure an attractive investment climate.
Improvement of R&D initiatives and clinical research should be the next focus for localization to allow Turkey to compete internationally. Since 2014, we allocated 210.68 billion Yen (10.769 billion TL) for R&D.

What are your foresights for the pharma industry in the world and in Turkey?
An aging population and increasing healthcare needs will determine the trends in the pharma industry not only for Turkey, but also around the world.
In Turkey, we continued our operations with our dynamic team of 80 individuals. Daiichi-Sankyo is on the threshold of major growth that will originate from cardiology and especially oncology products worldwide. This process will provide measurable growth in portfolio, employment and production in our Turkey operation.

How could regulation improve to give pace to the development of new drugs?
Innovator pharma companies acknowledge the concerns surrounding the affordability of innovative medicines and purchasing power issues facing healthcare systems under pressure from growing demand. The pharmaceutical industry is committed to supporting greater access and the sustainability of healthcare services.
Daiichi-Sankyo shares a common goal with all stakeholders: achieving rapid patient access to the latest, effective, life-saving medicines. Therefore, while recognizing the future position of innovative medicines, we work with governments and healthcare providers to enable better access to medicines and enhance sustainability.

What is your strategy and vision for the future?
Daiichi-Sankyo gives importance to Turkey in its future plans. We would like to develop our collaborations in Turkey through all areas that bring added value to human health and transform Daiichi-Sankyo Turkey into a regional hub to navigate into neighboring markets. For us, the most important indicators of localization are our compliance with the regulation and reliance on the economy of our country of operation, as well as developing value-added areas such as R&D, raw materials, clinical researches, and business partnerships beyond production. ■

Mehmet Goker

CEO
TR PHARM İLAÇ

How has the company developed since it was established in 2013?
We are a start-up in the true sense of the word, amongst a cluster of pharmaceutical companies that have long-established roots with more than 20 years in the industry. TR Pharm's main business is to in-licence originator products for Turkey, as well as the Middle East and Africa. A core principle upheld by TR Pharm is to be a medically-driven company, rather than just a distributor of generics. TR Pharm is also focused on specialty sectors, and stands out in oncology, haematology, rare disease, and, starting this year, CNS, with the potential to expand into rheumatology. Moreover, the products we licence are technologically advanced, and typically a first generic or super generic.

Could you elaborate on what are TR Pharm main areas of operation?
Besides in-licensing, a second pillar of TR Pharm's existence is our strong belief in R&D. Unfortunately, to measure with multinational level R&D, one needs billions of dollars of investment, so we decided to start with the "D" of R&D, looking into the development phase, especially in clinical studies. TR Pharm has a clinical department where we conducted a phase one study in the rare disease area in Turkey, in both FMF (Familial Mediterranean Fever) and Behcet's disease. This was the first in-human original molecule clinical study done in Turkey's history.
Finally, TR Pharm has begun a production facility, but we had to pull the brake on this investment due to macroeconomic issues. Factories are easily financed and built, but running a factory is a very cash-burning process that cannot be sustained without operating at high capacity or through product procurement guarantees.

How does Turkey fare as a destination for clinical trials in terms of the availability of patients/volunteers?
Doing clinical trials in Turkey is challenging, simply because Turkey has a universal health policy, and thus Turkey's citizens have access to free medicines through their social security. This raises the question of why anyone would want to take part in a clinical study, when the original product is available and free of charge? Moreover, there are many insurance related challenges, and finding candidates with the right profile is in itself a hurdle. Nevertheless, Turkey offers a large pool of patients for rare diseases, with a high proliferation of genetic diseases as a result of inter-family marriages.

How would you comment on the availability of capital and financing opportunities in Turkey?
Contrary to what people think globally, capital is available in Turkey, but the pharmaceutical industry is a very sophisticated business, so one needs to find investors who understand its intricacies. However, if a pharma company proves itself as an asset-driven and valued business, there will be private equity firms that will provide money, because Turkey is an attractive market.

What will be the main factors shaping the pharma industry in coming years?
Turkey is highly regulated, mirroring the European system, but it is also burdened by a foreign currency issue, on top of mandatory discounts. If we want to add value to the market in the future, our R&D needs to be supported by the authorities. If people are willing to pay 20 TL for a pack of cigarettes, we need to also unlock their willingness to pay for a pack of antibiotics. Unless the burden on the health budget is alleviated, the government remains limited in being able to support and finance R&D projects. Most of Turkish pharma companies are large-scale distributors, without conducting their own R&D, and even those operating into biotech are typically bringing drugs from overseas and doing the fill-and-finish here in Turkey. Investing in the drug substance manufacturing and APIs is a costly business, but the principles of economies of scale outset these interests. However, to add true value to the Turkish pharma industry, we need to get into R&D sooner or later, because innovation is the only way the pharmaceuticals industry will get meaningful profits and add value to their country. ■

To add true value to the Turkish pharma industry, we need to get into R&D sooner or later, because innovation is the only way the pharmaceuticals industry will get meaningful profits and add value to their country.

Zafer Toksöz

Chairman
ARVEN İLAÇ

Can you give an overview of Arven and the reasons behind the establishment of the company?
Arven is part of the Toksöz Group and was established in 2007 with a focus on developing inhalation and biotechnology products. Considering the rapidly changing dynamics of the global regulatory environment, in 2012, the Toksöz Group decided to start up Sanovel – the branded generic of the group - and Arven – a company dedicated to the development and manufacturing of inhalation products and biologics. Today, Arven strives to develop quality products for the global market and we are the first Turkish company developing biosimilars for global markets, including USA and EU.
Arven, a 100% Turkish capitalized pharmaceutical company, succeeded in developing the first Turkish patented dry powder inhaler (DPI) "Sanohaler" as a result of long lasting R&D activities, which is a significant milestone in Turkish pharmaceutical industry. Moreover, as a result of investments in biotechnology, Arven succeeded in creating Turkey's "from cell to finished biosmiliar product".

Can you elaborate on Arven's core capabilities and product portfolio?
Our core capabilities include production of therapeutic proteins, determination of quality of therapeutic proteins, head-to-head comparison with reference products, analytical similarity studies, bioassay studies, and receptor binding studies. One of the main products we offer to the market is a DPI device. The DPI was not created as a generic product, but rather a new and more effective drug delivery system (DDS). In addition to DPI products, we continue to invest in the necessary equipment for the R&D of different types of inhalation products.

What is usually the process and timeframe from developing a product to taking the product to market?
The idea of developing a DPI device came back in 2006 and the Sanohaler product was launched in 2013. It took us seven years to go to the market from scratch and we are planning to launch the Sanohaler in the United States in 2023.

Why is Arven focused on the development of inhalers and biosimilars?
The main aim of the company is to focus on specific product areas and especially products that are difficult to make. It was said that it was impossible to develop an inhaler drug delivery system and Arven decided to take on the challenge. The entire world is changing to biotechnologies. New products today are biologicals and the active ingredient is not through chemical syntheses, but the products extracted from a biological source. Biological products act more like antibodies. Realising that biologicals are the future of the industry, but without the capital to invest in developing new drugs, we decided to focus on the biosimilar space.

How does Arven find the balance between being sustainable in the market and having the room to innovate?
From a regulatory perspective, Turkey is possibly one of the toughest markets as the country does not have its own regulation system, but adheres to regulations from the FDA, Europe and other countries in the world. The government does support manufacturing in Turkey, but this does not mean that we have any advantage of getting to market. Arven follows the highest quality standards and regulations to make sure that we take the best products to market. The products we currently have in our portfolio are compatible with global standards. We are not only focused on the Turkish market, but can export our products around the globe.

What is Arven's vision and objectives moving forward?
Obtaining the investment needed to take our company global will take a significant amount of time in the Turkish market and thus we have made the strategic decision to become a CDMO. We have the knowledge, capacity and facilities to continue our activities as a company that produces biotechnology drugs as well as respiratory products for the international markets. ■

The main aim of the company is to focus on specific product areas and especially products that are difficult to make. It was said that it was impossible to develop an inhaler drug delivery system and Arven decided to take on the challenge.

Turgut Tokgöz

Secretary General
IEIS
The Pharmaceutical Manufacturers Association of Turkey

Could you briefly give us an overview of IEIS's mandate and evolution, identifying the key role that the association plays in the industry? What is IEIS's vision for the future?

The Pharmaceutical Manufacturers Association of Turkey (IEIS) has been contributing to the development of healthcare policies since 1964. We have 53 national and multinational members.

We cater to a diverse group of companies with different business interests, stretching from the production and imports of medicines to APIs. In this context, we are effectively involved in all areas of the pharmaceutical industry and assume an important role in establishing healthcare policies. We are an influential partner for policy makers in the development of legislation.

Our aim is to create a better ecosystem for R&D, innovation and value-added manufacturing that will strengthen the position of the Turkish pharmaceutical industry in the global market.

IEIS has developed new platforms, including a biotechnology platform and an exports platform. Would you like to elaborate on the need to bring together industry players under these umbrellas?

The Turkish Pharmaceutical Exporters Platform was established in by IEIS in 2012 with the aim of promoting the industry's high standards in international markets and increasing its competitiveness to make it a leading exporter in the global market. Our platform has 24 members today. Since its founding, we have been diligently working to promote our powerful and advanced pharmaceutical industry in international markets.

As a result of such efforts and the synergy created under the platform, pharmaceutical exports have been rising steadily. Turkey's pharmaceutical exports have reached US$ 1.4 billion.

We established the Turkish Biopharmaceuticals Platform at the end of 2016, with the aim of creating synergy in the field of biotechnology. The platform is comprised of 23 companies active in this field. Our efforts and activities are focused on creating a regulatory environment in line with needs, establishing an effective incentive scheme and ensuring a qualified work force.

What impact might the unfolding localisation policy have in terms of changing the dynamic between local and foreign players?

Turkey's localization efforts, under the leadership of the MOH, have produced many positive outcomes over the last three years. During this process, the industry has invested in new technologies, increased capacity utilization and employment, while imports have diminished. Long-term manufacturing contracts are also focusing on pharmaceutical exports.

IEIS deems the continuation of localization policies of great importance for our industry and therefore we support them.

The government has taken initiatives to boost growth in pharma and biopharma, whilst holding prices down through the cross-referencing system. How can sustainable access to healthcare be reconciled with the needs of the industry?

Needless to say, the government's pricing policies for the last 10 years have not been constructive for the industry. The expansion in social security coverage and improvement in health services, paving the way for higher accessibility to pharmaceuticals, has come at the expense of the industry. The resulting increase in public pharma spending has been curtailed by severe price controls.

Both the government and the industry have high ambitions to make Turkish pharma a leading global player. However, such a leading role requires increased R&D spending as well as investments in new technology, which in turn requires sufficient profitability and capital accumulation.

So, we definitely need a more balanced and sustainable approach from policymakers.

What prospects are in line for Turkey to become a biotech hub?

Very impressive investments have been made in the field of biotechnology in the last three to four years. Companies are working hard to enter the global biosimilars market with a long-term perspective. Given the rooted pharma production culture, we believe that Turkey will also be successful in this field.

The pipeline of companies active in biotech suggest that 41 products will be marketed by 2024.

In order for Turkey to compete effectively in this field, a supportive ecosystem needs to be established. Enhanced licencing regulation that will shorten time-to-market is of utmost importance. New incentive schemes geared towards more public funding would be of help, too. New patients should be encouraged to begin treatment with biosimilars produced in our country. ■

COMPANY/ INSTITUTION	WEBSITE
Abdi İbrahim İlaç San. ve Tic. A.Ş.	www.abdiibrahim.com.tr/en/
Acıbadem University Research Laboratory	www.acibadem.edu.tr/en/
Ali Raif İlaç San. A.Ş.	www.aliraif.com.tr
Arven İlaç San. ve Tic. A.Ş.	www.arvenilac.com.tr
AstraZeneca İlaç San. ve Tic. Ltd. Şti.	www.astrazeneca.com.tr
Atabay İlaç Fab. A.Ş.	atabay.com
Bilim İlaç San. Tic. A.Ş.	www.bilimilac.com.tr
Birgi Mefar İlaç San. A.Ş.	www.mefar.com
Centurion Pharma İlaç San. ve Tic. Ltd. Şti.	www.centurion.com.tr
Cinnagen İlaç Sanayi ve Ticaret A.Ş.	www.cinnagenilac.com.tr
Daiichi-Sankyo İlaç Tic. Ltd. Şti.	www.daiichi-sankyo.com.tr
Delta PV	www.deltapv.com/en/
Dem İlaç San. ve Tic. A.Ş.	www.demilac.com.tr
Deva Holding A.Ş.	www.deva.com.tr/en/
Drogsan İlaçları San. ve Tic. A.Ş.	www.drogsan.com
Eczacıbaşı Monrol Nükleer Ürünler San. ve Tic. A.Ş.	www.monrol.com.tr
Ege University Research and Application Center of Drug Development	argefar.ege.edu.tr
and Pharmocokinetics	www.ekinkimya.com
Ekin Kimya Tic. A.Ş.	www.ekinkimya.com
Ekol Lojistik	www.ekol.com
Era Pharma Analitik Çöz. ve İlaç San. Tic. A.Ş.	www.erapharma.com.tr/tr/iletisim/
Exeltis İlaç San. ve Tic. A.Ş.	exeltis.com.tr/iletisim
Farma-Tek İlaç San. ve Tic. A.Ş.	www.farma-tek.com
Florabio Teknoloji San. Ve Tic. A.Ş.	www.florabio.com.tr
Has biotech İlaç San. ve Tic. A.Ş.	www.linkedin.com/company/hasbiotech-ila-san-ve-tic-a-/
IEIS (Pharmaceutical Manufacturers Association of Turkey)	www.ieis.org.tr
Istanbul Technical University	www.itu.edu.tr/en/ituresearch/research/research-centers
Molecular Biology-Biotechnology and Genetics Research Centre	
Izmir Biomedicine and Genome Center (IBG)	www.ibg.edu.tr
Kansuk Lab. San. ve Tic. A.Ş.	www.kansuk.com
Koçak Farma İlaç A.Ş.	www.kocakfarma.com
Liba Laboratuarları A.Ş.	www.liba.com.tr/en/
Meksmar Natural & Health Products	www.meksmar.com
Nobel İlaç San. ve Tic. A.Ş.	www.nobel.com.tr
Platin Kimya	www.platinagro.com
Recordati İlaç San. ve Tic. A.Ş.	www.recordati.com.tr
Sabancı University Nanotechnology Research and Application Center	sunum.sabanciuniv.edu
Sanofi İlaç San. ve Tic. A.Ş.	www.sanofi.com.tr
Sanovel	www.sanovel.com
Santa Farma İlaç San. A.Ş.	santafarma.com.tr
TR Pharm İlaç San. Tic. A.Ş.	www.trpharm.com
TÜBİTAK MAM Genetic Engineering and Biotechnology Institute	gmbe.mam.tubitak.gov.tr/en
Tüm Ekip Pharmaceuticals	www.tumekip.com.tr
Turgut İlaçları A.Ş.	www.turgutilac.com.tr

This list intends to include just a representative sample of companies operating in Turkey's pharmaceutical and biopharmaceutical sectors, and as such it should not be considered a guide to take investment decisions.

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THANK YOU

We would like to thank all the executives and authorities that took the time to meet with us.
Also, special thanks to our partners at Pharmaceutical Manufacturers Association of Turkey (IEIS).

This year, GBR is also launching a digital platform with exclusive information that invites audiences to zoom into the company profiles of the major pharma and biopharma firms that make up the industry in Turkey.

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