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Rare Diseases and Orphan Drugs

There are approximately 6 to 8 thousand rare diseases in the world. It is estimated that 250 to 300 million people around the world and about 27-26 million people in Europe fighting against rare diseases; and 6 to 8 percent of the population in Turkey, accounting for roughly 5 million people,are affected by rare diseases.

Burcum Hanım, we would like to get to know you first.

I completed my undergraduate studies in the Faculty of Pharmacy at Hacettepe University. After completing my graduate studies in Pharmaceutical Tehcnologies at Hacettepe University in 2000, I began working in the pharmaceutical sector. Since then, I have worked in different capacities in various departments, such as R&D, business development and licensing as well as corporate communications.

In 2007, I completed my MBA in Global Management and Marketing at Bahcesehir University. This program allowed me to better understand global and internationalization operational dynamics and processes as well as their effects on our sector. In other words, I had the opportunity to enter our sector at the international level and to learn more on new pharmaceutical segments. I joined Celgene Turkey family in 2009. As of today, I am in charge of Regulatory Affairs and Market Access at Celgene.
My experience with orphan drugs started at Celgene.

My personal interest in rare and difficult areas in the sector, such as orphan drugs and the low awareness level of orphan drugs' added-value to the sector encouraged me to develop expertise in orphan drugs and allowed me to actively participate in developing our company's strategic objectives. I feel privileged for being a member of a company dedicated to delivering therapies for patients with unmet medical needs and for participating in national policies aimed to promote the development of orphan drugs in Turkey. I feel really lucky in this respect.

How can we define orphan drugs? For what kind of diseases are orphan drugs used?

An orphan drug is defined as a human medicinal product that is used to diagnose, prevent, or treat life-threatening or debilitating rare diseases. The European Commission defines rare diseases as a life-threatening or chronically debilitating diseases that are of such low prevalence that special combined efforts are needed to address them. As a guide, low prevalence is taken as prevalence of less

than 5 per 10,000 in the Community. Compared to other diseases; rare diseases have broader effects on patients' lives. In addition to their treatment, the diagnosis of rare diseases alone takes years and patients are exhausted by this process. Other differences, in the case of rare diseases, are that patient families and friends are deeply affected and marginalized by the long diagnosis and treatment processes, which are surrounded by uncertainties.

There are approximately 6 to 8 thousand rare diseases in the world. It is estimated that 250 to 300 million people around the world and about 27-26 million people in Europe are fighting against rare diseases; and 6 to 8 percent of the population in Turkey. This means that roughly 5 million people, within Turkey, are affected by rare diseases. Given the fact that some rare diseases are congenital, and that the rate of intermarriages in certain parts of Turkey are comparatively high, rare diseases can have a deep impact on public health. In other words, rare diseases do not only have a social dimension requiring a differentiated policy approach in terms of public health.

What is the position and market share of orphan drugs in the pharmaceutical sector?

With limited or even non-existence of therapeutic options available for those patients living with rare diseases, the promotion of research and development of orphan drugs is of crucial importance for increasing patients' quality of life and extending their life span. Orphan drugs offer a medical advantage where there is no alternative treatment and therefore create a crucial difference. Rare diseases and orphan drugs are a relatively unknown compared to other pharmaceutical areas. Orphan drugs were only recognized as a different category in the US in 1980, in Japan in 1993, in Australia in 1998 and in the EU in the 2000s. Every country offers different incentives to the orphan drug sector according to the country's needs. For instance, Australia offers 5-year long market exclusivity to orphan drug companies whereas it is 7 years in the US and 10 years in Japan. In addition, it should be noted that the orphan drug industry is one of the most innovative, technologically advanced and promising segments in the pharmaceutical sector.

What are the primary differences between companies focusing on orphan drug R&D and companies focusing on regular disease treatments?

Orphan Drug companies are highly innovative and their production is R&D intensive. As a result, local economies in which they are produced directly benefit from enhancements in infrastructure and medical and pharmaceutical innovation. However, orphan drug companies typically face greater research and development risks due to high uncertainty and complexity inherent to orphan drug development and commercialization. Research in the field of rare diseases is extremely complex, therefore the cost for companies that conduct research in new or little-known fields are very high. In addition to the research risks, there are major economic risks. In contrast to the conventional pharmaceuticals sector, the rare disease model cannot be based on economies of scale due to the limited number of patients they treat.

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The sustainability of orphan drug development depends on the ability of companies to remain dynamic and to innovate constantly and rapidly. In order to mitigate the risks inherent in the research, development, and commercialization of orphan drugs, companies require various incentives which will, not that would provide timely access to the market, enabling visibility and therefore continued investment.

How do you assess the orphan drug situation in our country? Can we say that patient access to drugs is sufficiently supported by the current regulations and decision makers?

As I mentioned previously, the orphan drug sector constitutes one of the most innovative and promising segments of the pharmaceutical industry and thus has

In the Health Industries Structural Transformation Program Action Plan prepared within the scope of 10th 5-Year Development Plan of 2014, it was decided to “create a capacity in our country for orphan drugs” and the Ministry of Health is committed to this issue. Therefore in the last few years, the public sector has acknowledged patients’ need for a robust National Orphan Drug policy framework to improved access to medicine and set some goals for rare diseases and orphan drugs within the scope of Turkey’s development strategies and action plans.

great potential for economic growth in Turkey, particularly in strengthening Turkey’s innovative capacity and achieving Turkey’s Vision 2023 development objectives in high value-added sectors. Turkey has taken many important steps and has made significant progress in the health sector in general. In terms of orphan drugs, for example, the National Orphan Drug Draft Guidelines were prepared by the Turkish Medicine and Medical Equipment Institution in 2010, and shared with the sector representatives for their comments. The Draft was last updated during the 2014 Rare Diseases and Orphan Drugs Symposium and Orphan Drugs Workshop organized by the Rational Drug Use Association, which included the attendance of all of the sectorial stakeholders.

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All these goals have been effectively linked to Turkey’s development strategies and action plans. All of these developments inform us about Turkey’s vision and more importantly encourage us. However, further progress is being challenged by the current policy environment, which has been adversely affecting the overall investment landscape, and impeding pharmaceutical companies’ production and investment decisions which in turn poses risks to patients’ access to orphan drugs. For instance, as a direct result of companies not being able to provide their products directly to the Turkish market, the Turkish Pharmacists Union imports numerous orphan drugs which could otherwise be supplied at relatively lower prices. This seriously affects our country’s health budget.

What can be done to improve the situation of orphan drugs in Turkey; what kinds of reforms can be made?

On 6 Nobember 2014, our Prime Minister announced the “Health Industries Structural Transformation Action Plan”. The plan states that, “a greater capacity for orphan drugs will be created and accredited research, testing and evaluation centers will work closely with local and international sector in order to be established.” Under the scope of this plan, there are significant cooperation and coordination opportunities for all stakeholders. For instance, it will be possible for a rare disease commission to be established under the MoH. It will also be possible to create a database that can be used for the purpose of searching registrations and other data collected from the current diagnosis and treatment centers. In cooperation with Orphanet it will be possible to sign an interface agreement that will allow for the creation of a national database. TUBITAK will be able to run and finance such a project.

Additionally, workshops can be organized to discuss the future steps for the establishment of the necessary infrastructure for orphan drugs with relevant stakeholders. During these workshops, rare diseases can be assessed in detail and classified as genetic and non-genetic. In accordance with our country’s needs and social structure, a more inclusive prevalence study can also be implemented. With the data collected from this study, the National Regulation (Guidelines and regulation) can be rapidly finalized and enacted. Finally, national policies can be developed regarding reimbursement, pricing and incentive policies. A Temporary provision system for products submitted for reimbursement after registration and a differentiated treatment of orphan drugs prioritizing review/abbreviated committee processes can be set up. Pricing incentives, such as current exchange rate application, mandatory discount exemption, and orphan drug market exclusivity (10 years) aligned with specific international norms can also be offered.

Another important recent development is the Turkish General Assembly’s 14 November 2014 approval of the second part of the draft law to establish Turkey’s Health Institutes Directorate. As a private-budget public legal

entity with scientific and administrative autonomy, the Health Institutes Directorate (TÜSEB) will be established to provide services in healthcare sciences and technologies under the Ministry of Health. TÜSEB will be responsible for the coordination of management and implementation of heathcare thechnologies decisions made by the Science and Technology High Council, conduct R&D, provide financial and scientific support to R&Ds, coordinate and incentivize them, monitor them, and develop programs and projects for this purpose. This widening of the scope of the Directorate to include rare diseases will be helpful to accelerate the process of creating national policies on orphan drugs and implementing necessary human and institutional infrastructure. For instance, if the Directorate itself conducts epidemiologic data gathering, which is crucial for fighting rare diseases, this will lay a scientific ground for rare disease policies and accelerate planned, ongoing and potential studies.

From a global perspective, what is your assessment of orphan drugs' future profile, can we be hopeful?

Rare diseases and orphan drugs are a special topic that has different regulations in other countries. As I mentioned previously, rare diseases are not only rare but also represent a public health problem. Diminishing life quality, productivity, and efficiency, frequent hospital visits, feeling of dependency and burden, and depression are all reflected on patients' relatives and negatively affect them. Families of children struggling against rare diseases are severely affected by this process. For this reason, many countries are offering incentives to support orphan drug development. Orphan Drug Laws have been enacted in the US in 1983, in Japan in 1993 and in Australia in 1998. The EU enacted the Orphan Drug Regulation (EC No. 141/2000) in 2000, creating the legal basis to increase orphan drug access and providing incentive system to support pricing, licensing, reimbursement and R&D in the EU member countries.

Other countries have followed the EU and created similar incentives systems. These legal regulations rapidly increased the countries' R&D capacities. For instance when looked at the EU countries:

Orphan drugs R&D investments in Europe increased 51 percent between 2000 and 2004 and 104 percent between 2004 and 2008. This means that R&D investments increased to 240 million Euros in 2004 from 158 million Euros in 2000; and reached 490 million Euros

In Europe, R&D investments in orphan drugs increased 51 percent between 2000 and 2004, and 104 percent from 2004 and 2008. This means R&D investments that were 158 million Euros in 2000, reached 240 million Euros in 2004, and 490 million Euros in 2008. From 2000-2008, employment in the orphan drugs sector increased by 158 percent, R&D focused employment increased by 161 percent. These developments increased the number of licensed orphan drugs in Europe from 8 in 2000 to 76 in 2014.

in 2008.2 Employment in the orphan drug sector doubled between 2000 and 2008 and increased by 158 percent. R&D oriented employment increased by 161 percent between 2000 and 2008.2 All these developments have led to an increase in the number of licensed orphan drugs in Europe from 8 in 2000 to 76 in 2014.3 The EU Orphan drugs regulations have not only supported large scale and well-known pharmaceutical company investments, but also promoted the development of new companies that focus on the R&D in the pharmaceutical value chain. These companies may be relatively small in terms of their size compared to well-known pharmaceutical companies but they present great potential for development of highly innovative orphan drugs. For example in 2005, 85 percent of orphan drug applications are done by small and mid-scale companies, which were relatively new in the sector. In conclusion, we can be hopeful as long as there is increased awareness on the part of public and public sector of orphan drugs and their particular value in pharmaceutical sector, and there is increased cooperation and coordination among all stakeholders in developing patient-oriented and long-term healthcare solutions.

[1] European Commission Health & Consumer Protection Directorate-General http://ec.europa.eu/health/ph_information/documents/ev20040705_rd05_en.pdf
[2] OHE Consulting Assessment of the Impact of Orphan Medicinal Products (OMPs) on the European Economy and Society (Commissioned by EBE-EuropaBio)
[3] Orphanet Report Series - Lists of medicinal products for rare diseases in Europe (January 2013)
[4] Orphan drug development across Europe: Bottlenecks and opportunities, Harald E. Heemstra et al; Drug Discovery Today (2008)