THE BALTICS

LITHUANIA

LATVIA

ESTONIA

2018

SPECIAL REPORT

LITHUANIA: HIDDEN SURPRISES

LATVIA: TURNING THE PAGE?

ESTONIA: A REMARKABLE OUTLIER

VIROTHERAPY: RETHINKING THE WAR ON CANCER

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Preface

While Lithuania, Latvia and Estonia have a lot in common – small, high-income economies and Eurozone members situated on the Eastern coast of the Baltic Sea – it would be inadvisable to consider the Baltic states as one homogenous block. Lithuania, for example, shares many similarities with neighboring Poland; Latvia takes its cultural cues from Russia; while Estonia exudes Scandinavian characteristics due to its proximity to Finland.

In healthcare and the life sciences too, the Baltic states differ greatly. Lithuania, the largest market of the three, has a historic expertise in laser technology which is contributing to a thriving homegrown biotechnology industry. Latvia, on the other hand, boasts a strong industrial base and sees increasing numbers of medical tourists each year, although its government is working to reform what is a stretched public healthcare system. Estonia, the smallest of the three nations by population, has bet big on the digital revolution, with all public healthcare records now stored using blockchain technology and a number of innovative start-ups in the digital health space.

This report explores the peculiarities of these small but promising markets, as well as the ways in which actors from across the Baltics are working together on issues such as regulatory harmonization for medicine approvals and innovation clustering to propel the region’s industry forwards. 🌍
Dear members of the international healthcare community,

As vice minister of health of Lithuania, I am proud to introduce the 2018 edition of the Baltics Healthcare & Life Sciences Review, which I consider an excellent opportunity to showcase the very real progress underway across the country in these fields.

Aligned with the European guidelines, the health standards of Lithuanians have been steadily improving over the past decade. In parallel, the pharmaceutical and healthcare industries have always stood steadfast as crucial allies in overcoming the challenges we face and in bringing added value solutions to move our health system forward. Lithuania holds great attributes to further heighten the quality of care offered to our population and its access. In this regard, Lithuania’s government will continue to work with the full spectrum of public, private and civic stakeholders to provide Lithuanian patients and their families with longer and healthier lives.

To ensure the sustainability and development of our country’s health system, Lithuania’s Ministry of Health is currently implementing several structural changes such as the recently approved National Drug Policy, among others. As a result, all stakeholders engaged in healthcare hold a common interest and a shared duty in supporting the progress of our health system and in strengthening the spirit of collaboration that has to define the Lithuanian health ecosystem.

With the Lithuania Healthcare & Life Sciences Review 2018, I invite all members of the global pharmaceutical and healthcare communities to take a close look at the opportunities Lithuania has to offer, and to consider how they can leverage their unique expertise and capabilities to support Lithuania’s healthcare vision.

Sincerely,

Ms. Kristina Garuolien, Ph.D
Vice Minister, Ministry of Health of Lithuania
Distinguished members of the healthcare and pharmaceutical sector,

As Minister of Health, it is my great honour to introduce the Latvian chapter of the 2018 edition of the Baltics Healthcare & Life Sciences Review, which I consider an excellent opportunity to showcase the very real progress underway across the country in these fields.

2018 undoubtedly presents a favourable window of opportunity for stakeholders to align in shaping a more modern and outcome-oriented health ecosystem in our country. There can be no doubt that Latvia’s public health system has now reached a critical juncture in its development, exemplified by the trache of truly transformative structural reforms that we have been implementing.

One area where we have been making particular strides has been in recapitalization of our national health system with the passage of an ambitious and forward-looking Healthcare Financing Bill that stimulates the creation of mandatory health insurance. This decisive move will go a long way to enhancing patient access to latest generation therapies, while, at the same time, guaranteeing the sustained economic viability of Latvian public health in the years to come.

In this context, designing and implementing innovative, efficient and sustainable healthcare approaches combined with an accelerated digitalization of medical services and the strengthening of our country’s primary care capacity emerge as strategic priorities of the Ministry of Health.

With the Baltics Healthcare & Life Sciences Review 2018, I invite all members of the global pharmaceutical and healthcare communities to take a close look at Latvia’s dynamism and what it has to offer, and to consider how they can leverage their unique expertise and capabilities to support the continuous strengthening of our country’s healthcare vision.

Sincerely,

Anda Čakša,
Minister of Health, Latvia
SNAPSHOT IN FIGURES
The Baltic States Compared

<table>
<thead>
<tr>
<th>BALTICS COMPARATIVE CREDIT RATINGS</th>
<th>Moody’s</th>
<th>S&amp;P</th>
<th>Fitch</th>
</tr>
</thead>
<tbody>
<tr>
<td>ESTONIA</td>
<td>A1</td>
<td>AA-</td>
<td>A+</td>
</tr>
<tr>
<td>LITHUANIA</td>
<td>A3</td>
<td>A-</td>
<td>A-</td>
</tr>
<tr>
<td>LATVIA</td>
<td>A3 (stable)</td>
<td>A- (stable)</td>
<td>A- (stable)</td>
</tr>
</tbody>
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OUT OF POCKET PAYMENTS

<table>
<thead>
<tr>
<th>% OF HEALTHCARE COSTS PAID OUT-OF-POCKET</th>
</tr>
</thead>
<tbody>
<tr>
<td>LATVIA</td>
</tr>
<tr>
<td>42%</td>
</tr>
<tr>
<td></td>
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</table>

ACCESS TO INNOVATION

<table>
<thead>
<tr>
<th>NUMBER OF MEDICINES</th>
<th>ACCESSIBLE MEDICINES</th>
<th>ACCESSIBLE (% OF TOTAL NUMBER)</th>
</tr>
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<td>UK</td>
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<td>102</td>
</tr>
<tr>
<td>GERMANY</td>
<td>135</td>
<td>109</td>
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<tr>
<td>SLOVAKIA</td>
<td>134</td>
<td>55</td>
</tr>
<tr>
<td>CZECH REPUBLIC</td>
<td>135</td>
<td>50</td>
</tr>
<tr>
<td>LITHUANIA</td>
<td>135</td>
<td>38</td>
</tr>
<tr>
<td>ESTONIA</td>
<td>135</td>
<td>30</td>
</tr>
<tr>
<td>POLAND</td>
<td>45</td>
<td>7</td>
</tr>
<tr>
<td>LATVIA</td>
<td>27</td>
<td>7</td>
</tr>
</tbody>
</table>

SALES DYNAMICS IN THE BALTICS TOTAL MARKET (2012-2018)

<table>
<thead>
<tr>
<th>VALUE (EUR)</th>
<th>ESTONIA</th>
<th>LATVIA</th>
<th>LITHUANIA</th>
</tr>
</thead>
<tbody>
<tr>
<td>2012</td>
<td>423,951</td>
<td>239,190</td>
<td>221,999</td>
</tr>
<tr>
<td>2014</td>
<td>462,557</td>
<td>257,336</td>
<td>249,576</td>
</tr>
<tr>
<td>2016</td>
<td>510,296</td>
<td>316,654</td>
<td>289,889</td>
</tr>
<tr>
<td>2018</td>
<td>526,808</td>
<td>363,827</td>
<td>309,019</td>
</tr>
</tbody>
</table>

LATVIA BELONGS TO THE CORE OF EUROPE

EUROZONE MEMBERS

OECD MEMBERS

NATO MEMBERS

Source: S&P, Fitch, Moody’s, LAWG, 2016, OECD, European Observatory on Health Systems 2017
SNAPSHOT IN FIGURES
The Baltic States Compared

LOW SPENDING TRANSLATES TO LOW HEALTH OUTCOME

Source: OECD, European Observatory on Health Systems 2017

*Amenable mortality is defined as premature deaths that could have been avoided through timely and effective health care.

Source: OECD, European Observatory on Health Systems 2017
SNAPSHOT IN FIGURES
The Baltic States Compared

EVOLUTION OF THE BALTICS’ GENERICS MARKET
(2011-2017)
Source: SoftDent

DYNAMICS OF RX AND OTC DISPENSING TYPES IN BALTIC STATES

VALUE (EUR ‘000s)

<table>
<thead>
<tr>
<th></th>
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<th></th>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Rx</td>
<td>702,050</td>
<td>738,127</td>
<td>768,681</td>
<td>807,963</td>
<td>864,184</td>
<td>934,247</td>
<td>968,950</td>
<td>1,012,462</td>
</tr>
<tr>
<td>OTC</td>
<td>142,538</td>
<td>147,013</td>
<td>159,013</td>
<td>161,507</td>
<td>172,398</td>
<td>182,592</td>
<td>189,103</td>
<td>195,275</td>
</tr>
</tbody>
</table>

Source: SoftDent
For over 90 years, we have been helping people with diabetes to live their lives with as few limitations as possible. Our innovation has led to a broad portfolio of delivery devices and diabetes treatments that can enable better control of blood glucose levels.

But our work is far from over. Too many people with diabetes continue to develop serious and costly complications that could have been prevented or delayed. Some people with diabetes lose focus on diet and exercise. Others stop taking their medicine because it does not become part of a daily routine, or because they fear hypoglycaemia.

This is why we will continue to discover and develop treatments that meet the individual needs of people with diabetes. By doing so, we work towards our ultimate goal – defeating diabetes.

Learn more about our innovations at novonordisk.com/rnd

To the uninitiated, the Baltics, with its combined population size of just over 6 million inhabitants, might, at first glance, appear well suited to treating as a single, all-encompassing marketplace. To do so, however, would be to ignore sharp socio-economic and structural divergences that define and shape the market momentum of each of the three states.

“From a Western European standpoint, there is all too often a tendency to think of the Baltics as a single homogenous block. Such an approach would be, frankly, misguided. We’re actually talking about three distinct cultures with rather different histories and internal dynamics. Even in Soviet times, those cleavages were still apparent,” confides Ainars Kravalis, Baltic Country Manager of Wörwag Pharma. He strongly counsels against any comparison with the Balkans, which unlike the Baltics, underwent a considerable period of unification prior to splintering into separate nation states.

Firstly, there are some very obvious structural differences. “Latvia, for instance, is much more industrial in its infrastructure and still exudes some of the vestiges of a tightly regulated, planned economy. Lithuania lacks a historically ingrained chemical-industrial base, but makes up for it with a thriving biotech scene, while Estonia’s home-grown component is limited by the paucity of its size and instead differentiates itself through the harnessing and application of advanced digital technologies,” he points out.

Victor Shatz, chairman and owner of medical device importer and distributor, Fanex, heartily agrees. “The pharma industry in Estonia is tiny and mostly connected to the universities. Latvia enjoys what I would describe as a real classical pharma industry, but comparatively few biologics-dedicated entities, while Lithuania is noticeably stronger in bioprocesses and biopharma.”

Then there are legal and regulatory differences to factor into the equation. “First and foremost the way each government goes about managing healthcare is quite distinct. The overall attitude, the financing and the organization of the healthcare apparatus change radically from one country to the other. If you look at Estonia, there is little real willingness by anyone to develop a strong private healthcare system as you can generally access decent public healthcare easily. This is, for instance, certainly not the case in Latvia where the basic public healthcare system is very limited and requires significant out-of-pocket payments. As a result, private healthcare has moved in to fill the gaps. Lithuania lies somewhere in between on the scale and to some extent it resembles the Polish healthcare system with very strong political influence,” observes Teva’s general manager for the Baltics, Janis Meiksans.
Naturally these regulatory idiosyncrasies also translate into variations in reimbursement and market authorization decision-making. “There’s been quite a lot of noise about harmonized procurement and regulatory convergence, but we’ve only really seen it yet in very specific niches such as vaccines,” notes Martynas Jocys, marketing director for the Baltics and general manager of the Lithuanian affiliate at AstraZeneca. “Right now, we have to draw up bespoke dossiers and strategies across all of our therapeutic areas. If we take lung cancer as an example, Tyrosene-Kinase Inhibitors (TKIs) have been part of the standard care in Lithuania and Estonia for four or five years, but Latvia is not there yet, and TKIs remain without reimbursement.”

But over and beyond the rules of the game, there are additionally underlying behavioural and cultural divergences that further flavour the business-operating environment of each state. “I would say that Lithuania is also more conservative in mentality given the strong catholic influence. This is played out when it comes to the local style of doing business. There’s wariness towards newcomers and a tendency to stick with tried and tested suppliers rather than to shop around for the best deal. We perceive a strong loyalty towards existing relationships so, if you are a latecomer to the party, you have a hard task on your hands dislodging your competitors. Conversely once you have managed to establish a relationship, then it will most likely prove enduring so long as you manage to adequately fulfil your side of the bargain,” reasons Janis Biezbardis, chairman and owner of medtech supplier, Farmeko.

The regional socio-political orientations of each Baltic state also somewhat muddy the water. Catholic Lithuania enjoys many cultural linkages with Poland, while Estonia possesses strong financial and ethnic ties to Finland and Latvia leverages its deep Russian diaspora to forge close economic bonds with its larger neighbour.

“Generally, when pharma multinationals determine where to place investments within the Baltics, they tend to follow a certain type of business logic. Companies that are very Western in their corporate culture might feel more comfortable going through Estonia because the operating environment has Scandinavian characteristics and way of doing business is almost Finnish in style. On the other hand, firms that are seeking volume sales will be more attracted by Lithuania’s slightly larger population and market size. Latvia offers an altogether different prospect. The country’s industrial heritage in chemistry and chemical manufacturing convert into skilled human capital. The local Russian diaspora also means the Latvian market can be a good gateway from Europe into Russia and the CIS and vice versa,” concludes Roche’s general manager for Latvia, Rauls Velins.

Certainly this calculation rings true for Farmeko. “At the end of the day, we have found that Estonia is easier to enter than Lithuania because price levels are a bit higher, they were quicker to introduce the euro currency and we can call upon the services of a dependable Finnish company, Tamro to handle our in-country distribution. In Lithuania, we have to compete with many entities importing from Poland and the barriers to entry are higher. The fact that the market is bigger also tends to attract in a proliferation of players so the competition tends to be more intense… Everyone wants to have skin in the game,” recounts Biezbardis.

Ultimately, all of these factors compel successful companies to adapt their market offerings accordingly. “We find it certainly pays to adopt tailor-made, localized go-to-market strategies that reflect the real business ecosystem on the ground. A one-size-fits-all, cookie cutter approach is always likely to fall short out here. Indeed, when I go to our global management board, I always present 4 business plans: a bespoke strategy for each Baltic state and an integrated pan-Baltic outlook,” argues Kravalis.
LITHUANIA
TOP 20 PHARMA COMPANIES IN LITHUANIA BY VALUE (2017)

<table>
<thead>
<tr>
<th>#</th>
<th>CORPORATION</th>
<th>VALUE EUR</th>
<th>GROWTH YoY</th>
<th>MARKET SHARE</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>JOHNSON &amp; JOHNSON</td>
<td>34,955,837</td>
<td>62.64%</td>
<td>6.28%</td>
</tr>
<tr>
<td>2</td>
<td>BERLIN CHEMIE</td>
<td>34,186,891</td>
<td>-2.65%</td>
<td>6.14%</td>
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<tr>
<td>3</td>
<td>NOVARTIS</td>
<td>29,925,646</td>
<td>-0.41%</td>
<td>5.38%</td>
</tr>
<tr>
<td>4</td>
<td>TEVA</td>
<td>29,399,653</td>
<td>0.22%</td>
<td>5.28%</td>
</tr>
<tr>
<td>5</td>
<td>PFIZER</td>
<td>24,589,769</td>
<td>-9.44%</td>
<td>4.42%</td>
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<tr>
<td>6</td>
<td>SANDOZ</td>
<td>23,883,131</td>
<td>2.79%</td>
<td>4.29%</td>
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<tr>
<td>7</td>
<td>SERVIER</td>
<td>23,792,565</td>
<td>-9.60%</td>
<td>4.28%</td>
</tr>
<tr>
<td>8</td>
<td>SANOFI</td>
<td>22,703,351</td>
<td>2.05%</td>
<td>4.08%</td>
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<tr>
<td>9</td>
<td>GLAXOSMITHKLINE</td>
<td>21,307,518</td>
<td>-6.31%</td>
<td>3.83%</td>
</tr>
<tr>
<td>10</td>
<td>KRKA</td>
<td>20,824,640</td>
<td>4.47%</td>
<td>3.74%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>#</th>
<th>CORPORATION</th>
<th>VALUE EUR</th>
<th>GROWTH YoY</th>
<th>MARKET SHARE</th>
</tr>
</thead>
<tbody>
<tr>
<td>11</td>
<td>ABBVIE</td>
<td>17,543,266</td>
<td>0.28%</td>
<td>3.15%</td>
</tr>
<tr>
<td>12</td>
<td>ROCHE</td>
<td>16,236,514</td>
<td>6.16%</td>
<td>2.92%</td>
</tr>
<tr>
<td>13</td>
<td>BAYER</td>
<td>15,173,923</td>
<td>2.18%</td>
<td>2.73%</td>
</tr>
<tr>
<td>14</td>
<td>BAXTER</td>
<td>14,053,842</td>
<td>48.09%</td>
<td>2.53%</td>
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<tr>
<td>15</td>
<td>NOVO NORDISK</td>
<td>13,690,612</td>
<td>9.20%</td>
<td>2.46%</td>
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<tr>
<td>16</td>
<td>ASTRazenECA</td>
<td>12,061,207</td>
<td>-19.47%</td>
<td>2.17%</td>
</tr>
<tr>
<td>17</td>
<td>MSD</td>
<td>10,034,870</td>
<td>4.20%</td>
<td>1.80%</td>
</tr>
<tr>
<td>18</td>
<td>GEDEON RICHTER</td>
<td>9,452,798</td>
<td>11.41%</td>
<td>1.70%</td>
</tr>
<tr>
<td>19</td>
<td>ELI LILLY</td>
<td>8,635,916</td>
<td>-9.09%</td>
<td>1.55%</td>
</tr>
<tr>
<td>20</td>
<td>MYLAN HEALTHCARE</td>
<td>7,600,536</td>
<td>0.62%</td>
<td>1.37%</td>
</tr>
</tbody>
</table>

LITHUANIA PHARMA MARKET - DISPENSING TYPES

- Rx, not reimbursed
- Rx, reimbursed
- Medical supply
- Food supplement
- OTC

Source: Softdent, PharmaZOOM, 2017

LITHUANIA EPIDEMIOLOGICAL PROFILE

39,764 DEATHS

- CARDIOVASCULAR DISEASES 56%
- CANCER 21%
- EXTERNAL CAUSES 8%
- OTHER CAUSES 7%
- DIGESTIVE SYSTEM 5%
- RESPIRATORY DISEASES 3%

Source: OECD, European Observatory on Health Systems 2017
UNVEILING A NEW NATIONAL DRUG POLICY

Kristina Garuoliene, vice minister at the Ministry of Health of the Republic of Lithuania, explains the cornerstones behind the new National Drug Policy approved in August 2017, the commitment of the Ministry to ensuring Lithuanian patients have access to the latest high-quality medicines regardless of their location or spending power.

HCLS: What were your initial goals, aspirations and priorities upon assuming your current position as vice minister of health last year?

KRISTINA GARUOLIENE (KG): My responsibilities are focused on the pharmaceutical area. It is important to mention that Lithuania was lacking a National Drug Policy in the past and, therefore, my main priority was the elaboration of a new one fully aligned with European standards. In this sense, I am delighted to share that a National Drug Policy was recently approved by our minister of health in August 2017 and should stay in place for the next decade, which will give all stakeholders a long-term view of the pharmaceutical sector in Lithuania.

HCLS: Can you tell us a bit more on the major priorities and ambitions behind this National Drug Policy?

KG: The cornerstone of this National Drug Policy is to sustainably offer universal healthcare coverage to all Lithuanians ensuring their access to the latest as well as highest quality medicines regardless of location or spending power.

Firstly, as aforementioned, reducing patients’ co-payments through pushing down drug prices is one of the main strategic goals behind this new policy in order to increase the patients’ access to the needed medicines. Secondly, improving the rational use as well as prescription of medicines is a key topic in this plan. There is a consumption trend in Lithuania in which pharmacists give prescription medicines to patients without an actual prescription. This can be dangerous for those patients who are purchasing a drug without a healthcare professional’s support. In this sense, since 1st of November 2017, the law allows the Ministry to send mystery shoppers to the pharmacies to ensure the correct commercialization of drugs. This measure has been unpopular because now patients need to get prescriptions to be able to take the drug that they were taking without prescription in the past; nevertheless, I believe that this is needed to be in accordance with European regulation as well as to ensure that patients take the right drug.

Thirdly, we aim to foster the use of generics in the country since some healthcare professionals and patients in the country do not believe that generic molecules are as effective as originators. In this area, we are collaborating with the industry to educate doctors and patients about the effectiveness of generic drugs; this will help the government to achieve a better sustainability of the public health funds.

HCLS: How has this new National Drug Policy been perceived by healthcare stakeholders in Lithuania?

KG: The elaboration process of this new policy was based on active roundtables with all the different healthcare stakeholders from government institutions to patients and industry associations. Obviously, it was really challenging to find common ground and there was not a full consensus in certain topics; but, overall, I am delighted to confirm that we count on the support of all the healthcare actors in the country.

“THE CORNERSTONE OF THIS NATIONAL DRUG POLICY IS TO SUSTAINABLY OFFER UNIVERSAL HEALTHCARE COVERAGE TO ALL LITHUANIANS”
Lithuania’s fledgling biotech sector has grown by between 20 and 25 percent over the last five years and accounts for over one percent of the entire country’s GDP. Key industry stakeholders are, however, split on whether Lithuania truly holds the potential to become a biotech hub that can stand alongside nations such as Singapore.

Lithuania has been ambitious in its plans to develop its biotech industry in recent years, with business, scientists and the government signing a resolution in May 2017 establishing the objective of making Lithuania a hub of health technologies and biotech innovations of Europe by 2020. More recently, in 2017 a EUR 200 million investment in three state-of-the-art facilities was announced that the country hopes will establish it as a bio-economy.

Prof. Vladas Bumelis, commonly regarded as one of the forefathers of Lithuanian biotech and the man coordinating the construction of these new facilities, explains that “One facility will produce large amounts of protein medicine from microbial cells through genetic engineering, another one will produce medicine from the cells of mammals. The third factory will be for performing cell therapy.”

Bumelis is forthright in his opinion that Lithuania and biotech are a good match, asserting that, “In general, the biotechnology sector very is suitable for Lithuania as it does not require large resources, except for knowledge, technologies – which you can invent yourself – and experts.” Bumelis continues, “in the future, everyone will talk about Lithuania as a country with a bio-economy, just as Switzerland is the country of the best quality watches and banks. We need to build our country according to what we are able to do and what we can do, concentrate on that, and not rush about in different fields of activity.”

Kristina Garuoliene, Lithuania’s vice minister of health, is similarly optimistic on the country’s biotech potential, noting that “Lithuania can lay claim to a historical legacy of biotechnology manufacturing through Biotechna, which was acquired by Teva back in 2004. As a result of this heritage, Lithuania possesses a certain amount of skilled talent and human capital ready to serve the industry in this arena. When you juxtapose this knowledge pool with the infrastructural capabilities that we have, then the idea of Lithuania cultivating a vibrant biotech space becomes more realistic. Moreover, it is current government policy to make some regulatory adjustments to render the country more appealing to this category of inward investment flows.”

Mantas Katinas, general manager of Invest Lithuania, is also keen to highlight specific biotech success stories as cause for confidence. He posits that, “Some of the most
prominent success stories in Lithuanian life sciences come from biotech. Teva and Thermo Fisher Scientific are companies with turnovers of around EUR one billion annually and both are ranked among the most profitable companies in the country. Thermo Fisher Scientific has established its center of excellence for molecular biology here and with almost 100 researchers employed at the facility, the company has the biggest private R&D center in the Baltic region. Employing almost 800 people in the Lithuanian facility, the company astounds with its lean management and has recently received a Shingo prize, rewarding its accomplishments."

Furthermore, as Romanas Ramauskas, manager of business development at UAB Biotechnologijų Parkas and chairman of the Lithuanian Association of Biomedicine and Biotechnology Companies, points out, although Lithuanian biotech companies are not yet numerous, many have become very profitable and are already contributing significantly to the national economy. He declares that, “At least 12 of the 25 companies active in the biotech sector generate substantial revenue and profits. A proportion of the companies within the sector are only at the stage of investing into research (which may take many years); hence they cannot boast of financial results as yet. The third category of companies within the sector is the beginners (startups). These 25 companies have just over 1,600 employees; nonetheless, Lithuania generates over one percent of GDP from biotechnologies. This exceeds Switzerland (0.91 percent) and the USA (0.43 percent).”

However, not all stakeholders are quite so ebullient on the issue of Lithuania’s potential as a biotech hub for Europe. Audrius Tutlys, Teva’s country manager in Lithuania, cautions that although, “Lithuania has officially expressed grand ambitions to become a European center for biotechnology by 2020, in my opinion, this still remains very much an aspiration rather than a hardcore reality on the ground.” Tutlys continues, “Ultimately, industry is going to require rather more support from the authorities in this direction if we are to really raise Lithuania’s positioning as an attractive, competitive and compelling destination country for FDI investments in the biotech world.”

LITHUANIA HAS OFFICIALLY EXPRESSED GRAND AMBITIONS TO BECOME A EUROPEAN CENTER FOR BIOTECHNOLOGY BY 2020, IN MY OPINION, THIS STILL REMAINS VERY MUCH AN ASPIRATION RATHER THAN A HARDCORE REALITY ON THE GROUND.

Also presenting a rather more circumspect point of view is Leonas Kalėtinas, executive director of the Lithuanian Innovative Pharmaceutical Industry Association (IFPA), who points out that while the aim of positioning Lithuania as Europe’s biotech center by 2020 is laudable, “it is important to manage expectations around this topic because, right now, this is still very much still in the planning phase and the requisite capabilities needed to attain this objective are not yet in place.”

Whether or not Lithuania can actually deliver upon its lofty aspirations remains to be seen, but the country’s ambitiousness and willingness to aim high cannot be denied. As Vladas Bumelis concludes, “If one does not have vision or a futuristic approach, then there would be no ideas or wishes to do something that has never been done before. I believe that we, Lithuanians, should be leaders, and that we should move forward instead of always complaining that someone has overtaken us.”

BIOTECH IN LITHUANIA

1% of GDP
25% GROWTH
HISTORICAL COMPETENCES AND GROUNDBREAKING RESULTS IN

BIOMOLECULAR ENGINEERING
BIOCHEMISTRY
EPIGENETICS
PROTEIN ENGINEERING

Source: Invest Lithuania, 2017
HCLS: What is the mandate of the SMCA as regulator for Lithuania, the biggest market in the Baltics?

GINTAUTAS BARCYS (GB): The SMCA is the Lithuanian institution in charge of controlling and surveillance pharmaceutical activities in order to ensure that only good quality, safe and effective medicinal products are available to the Lithuanian population.

HCLS: Just how transparent is the Lithuanian life sciences and healthcare sphere today?

GB: It is well known that Lithuania was facing some transparency issues in the pharmaceutical industry a few years ago, especially regarding financial help to physicians and other healthcare professionals. Nonetheless, this situation has substantially improved over the course of recent years. Therefore, we amended our law to force companies to disclose information about programs of market authorizations that are developed with Lithuanian healthcare professionals, which includes financing activities of the scientific international conferences. As a consequence, this law has enhanced the transparency in the Lithuanian pharmaceutical market.

HCLS: CROs are an important area of foreign investment into Lithuania and one of the main tasks of the SMCA is the oversight of clinical trials. What can be done to promote activity in this segment?

GB: The clinical research arena presents several opportunities, but it is still quite under-developed due to the low collaboration between large hospitals and clinics in the countryside. I believe that we should build up a solid network of clinical trials in Lithuania together with our neighbouring countries in order create a regional clinical development hub in the Baltics resulting in synergies and benefits for all the stakeholders from industry to national governments and patients. From the SMCA standpoint, we are already fostering such regional cooperation and, indeed, we are currently participating in voluntary procedures at the European level for assessment of applications of clinical trials.

HCLS: How big an issue are drug shortages and what steps can be taken to enhance security of supply?

GB: It is a reality that we were facing, and still do face, worrying shortages of some medicines in the market due to parallel exports, amongst other causes. In this sense, we have recently started to implement a monitoring system to track those drugs that are present in Lithuania in order to early indicate and quickly react in front of any possible shortage. The outcomes of this initiative have been really positive and we have substantially reduced permanent medicine shortages. Nevertheless, such a monitoring program would not be possible without the participation of private stakeholders such as wholesalers and pharmaceutical manufacturers, who submit weekly and monthly reports to us about their stock, the number of packages sold to the pharmacies, among other information.

Gintautas Barcys, director of the State Medicines Control Agency under the Ministry of Health of the Republic of Lithuania (SMCA), sheds light on some of the key issues afflicting Lithuanian pharma.

**INJECTING RESILIENCE INTO THE MIX**

Gintautas Barcys
SMCA

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**BALTICS MARKETING AUTHORIZATIONS COMPARED**

Source: ZVA, 2016

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Seemingly eternally overshadowed by the larger, glitzier Polish mega-market next door, Lithuania’s healthcare and life sciences sector enjoys an ever-increasing role in the national economy, today accounting for roughly four percent of GDP with a somewhat surprising one percent sourced directly from a budding domestic biotechnology sector. “Indeed, life sciences related goods and services may not yet account for a big percentage of total national exports, but there can be absolutely no doubt that this is a sector is in high growth mode currently registering an enviable 25 percent per annum to be precise,” exclaims Daina Klepone, managing director of Enterprise Lithuania.
Mantas Katinas of Invest Lithuania is equally enthusiastic. “For a number of years, life sciences companies in Lithuania have been ranked amongst some of the most profitable ventures in the country. With high-value added production, these companies contribute greatly to national prosperity with some 90 percent of total pharmaceutical and medical production exported to over 100 countries... It therefore should come as no surprise that these sectors rate highly on the government’s agenda for further investment and are increasingly considered as strategic industries,” Katinas continues.

Certainly there is much to be positive about. The value of local life sciences more than doubled in the period 2010 to 2016, topping an annual figure in excess of EUR 500 million. Nowadays, Lithuania can lay claim to more than 300 pharma and medical device manufacturers while the local talent pool also raises eyebrows with some 2,400 fresh life sciences graduates coming on stream every year.

“With long-standing historical competences in molecular biology and enzymology, a well-developed R&D infrastructure and talented labor pool, that belies its miniscule market size on the European map, Lithuania possesses many reasons and parameters to be able to mature as a strong and fully-fledged life sciences hub that can really hold its own in international circles,” ventures Katinas.

Clearly the local operating environment and infrastructure base carry much appeal for any external actor seeking to enter the life sciences sector. “Lithuania represents a tremendously welcoming business ecosystem with convenient logistics,” Dalia Klepone, managing director, Enterprise Lithuania

Furthermore, there is the country’s well-matured research infrastructure base concentrated in the cities of Vilnius and Kaunas and encompassing the Santara and Santaka science valleys along with stand-out institutions such as Vilnius University Hospital, Kaunas University of Technology and the Lithuanian University of Health Sciences. “Don’t forget that with five integrated business and science valleys, Lithuania is towards the head of the pack when you start talking about concentration of open R&D infrastructure. We actually rank tenth in the world for R&D personnel per capita with 16 academic institutions, 15 R&D centers and a catchment pool of over 23,000 researchers,” laughs Katinas.

Moreover there are a whole host of other attributes that render doing business a breeze such as the country’s advanced ICT ecosystem. As Dalia Grybauskaitė, Lithuania’s first ever female president, never hesitates to point out, “Our nation is among the global leaders in information and communications technology infrastructure: we enjoy the world’s fastest fiber internet and Europe’s largest 4G mobile network.” Little wonder, then, that Lithuania ranks 16th in the World Bank’s ‘Doing Business Index’ ahead of heavyweight economies such as Germany and Ireland.

Unsurprisingly, international investors do seem to have taken the bait. In little over a decade, Lithuanian life sciences has undergone a dramatic process of globalization with star local outfits being snapped up by big name MNCs. Teva’s purchase of local biopharma player Biotecha, MOOG’s acquisition of syringe pump manufacturer Viltechmeda, Thermo Fisher Scientific’s
The distinction is that, whereas finding pockets of new growth in Western Europe has become rather challenging, Lithuania, with its sustainable and predictable economy, still has some growth-room left to tap into,” reasons Janis Kalejs, Mylan’s country manager for the Baltics.

Valeant’s general manager for the Baltics, Tomas Liesis makes a very similar assessment. “This is a tiny market, but, at the end of the day it is nonetheless dynamic and that is why multinationals are keen to include it as part of their operations. Lithuania is well aligned with European norms, but simultaneously promises decent growth expectations as part of the normal market maturation process and development trajectory. 15 years ago this region was considered an emerging market and, though we won’t be seeing a return of those days of heady 20 percent growth rates, it is fair to say that the Baltics are typically still growing a little bit faster... While many companies have seen their revenues shrinking slightly in the more mature...
LOPSIDED PUBLIC HEALTH: HIGH COVERAGE, BUT SOARING CO-PAYMENTS

At a first glance, Lithuania’s public health scenario looks wrought with contradiction. On the one hand, citizens enjoy widespread care coverage for a broad package of services with a single-payer, compulsory health insurance system largely funded through the National Health Insurance Fund (NHIF), ensuring recourse to treatment for even economically inactive population groups. On the other hand, out-of-pocket payments constitute a disproportionately large share of the national drugs bill, with many patients compelled to shell out the full cost of both prescribed and over-the-counter medications.

“Unfortunately Lithuania is notorious amongst its peers for having one of the lowest percentages of total pharmaceutical sales covered by public funds and we are ranked 29th out of 35 European countries in this regard,” laments Novo Nordisk general manager for the Baltics, Marijus Valatka. “With the annual drugs bill coming in at around 1.5 percent of GDP, only a mere 0.6 percent is provided for by the state leaving a shortfall of 0.9 percent to be made up through private means,” he calculates.

In short, there is a yawning discrepancy between the ratio of state funding of pharmaceuticals in comparison with levels of public expenditure on health services in general. Why might this be? A number of stakeholders are quick to point out that Lithuania pays comparatively more for off-patent products than many of its peers and that this is pushing up out-of-pocket expenses when the national purse is cash-strapped. “According to a benchmark study carried out by a third party, Lithuania actually has higher prices for generic medicines than the European average so correcting this imbalance is going to be fundamental if we are to make any headway in scaling down co-payments rates,” observes Leonas Kalėtinas, executive director of the Lithuanian Innovative Pharmaceutical Industry Association (IFPA).

Others, however, are adamant that the root of the problem is wasteful use of the existing resource base. “Overall expenditure is not quite as problematic as people often suggest. The amount of money that the state makes available for public health is actually rather reasonable when set against the rest of the region... Where we think there can be considerable progress is instead in the efficient allocation of these resources by channeling them in directions where they can wield maximal impact,” shrewdly affirms Lukas Savickas, adviser to the Prime Minister on health policy.

Rūta Pumputienė, head of the Local American Working Group (LAWG) of innovative pharma companies somewhat agrees. “I would like to stress that the exorbitant level of co-payments in Lithuania is not only a consequence of insufficient financial resources, which is a phenomenon being experienced by healthcare systems all across Europe, but also a product of the inefficient manner in which the funds are being expended and the woeful lack of effective health budget planning,” she concurs. “While the health burden is evermore weighty, as reflective of an aging population and the spread of lifestyle-related, chronic conditions, the Ministry intends to treat patients in the same manner as previous years without any real strategic foresight and forward planning,” she adds.

Certainly evidence of inefficiencies abound. In terms of physical resources, there is a general oversupply of hospitals and hospital beds. The number of curative care beds, for instance, is the second highest in the EU (608 versus 418 per 100 000 respectively) while the country also boasts a considerably higher ratio...
of physicians (4.3 per every 1,000 inhabitants) than the EU average (3.6). “Lithuania’s shrinking population and a tendency towards urbanization has left many rural communities with a large underutilized hospital capacity offering a broad set of services that is often duplicated elsewhere and you have to wonder whether keeping these assets running is the best use of public money when the patient needs would seem to be elsewhere and when, in some scenarios, home care could generate better health outcomes,” muses Linas Dičpetris, EY’s advisory services leader for the Baltic States.

While he acknowledges that reforms by recent government administrations have sought to shift care to outpatient and primary care services, cluster hospitals and re-profile excess curative wards into nursing, geriatric and palliative care spaces so as to better meet the country’s evolving patient profile, he notes that the political consequences of doing so are challenging.

“The crux of the matter is that there is a mismatch between the expectations of the public and the raw ability of a country of the population size and GDP of Lithuania to be able to pay. The relatively large hospital capacity and fact that there are no user fees for publicly reimbursed medical services tends to lead to excessive hospital consumption, and then we find there is not enough public money to adequately finance the national drugs bill. There clearly has to be an adjustment and rationalization, but enacting such changes will be unpopular amongst a public that has grown used to a certain scenario,” explains Dičpetris.

Meanwhile other indicators also suggest that Lithuania’s public healthcare offering is underperforming on a number of counts. Life expectancy in Lithuania is the lowest in the EU, six years below the EU average (74.6), while mortality rates for the two leading causes of death – ischemic heart disease and stroke – exceed the EU averages by four and two times respectively. Indeed, OECD and European Commission statistics for 2017 demonstrate that Lithuania has among the highest rates of thirty-day mortality within the EU after admission to hospital for a heart attack and stroke, and that the country’s hospitals also register some of the highest rates of antimicrobial resistance (AMR) in the Union.

**PUBLIC FUNDING OF HEALTH AND PHARMACEUTICALS**

Lithuania does well in terms of using state expenditure to fund healthcare services, where it exceeds EU averages, but performs badly in terms of state funding for pharmaceuticals.

**REIMBURSEMENT: READY TO DRAIN THE SWAMP?**

One way to rationalize public health spending on pharmaceuticals would, of course, be to have reliable mechanisms in place to objectively evaluate the comparative merits of reimbursing one drug over another. “Our studies reveal that the current legal regulation governing reimbursable pharmaceuticals is inefficient and results in higher prices for both consumers and the state... The old system of reimbursable pharmaceuticals resembles a stagnant swamp into which the water neither flows nor drains. I say this because it is tremendously difficult to get on the pharmaceutical reimbursement list in the first place and, once you’re there, it’s well nigh impossible to get kicked off,” declares Šarūnas Keserauskas chairman of the Competition Council. “We recommended there should
be a systematic way of looking at the list and renewing it based on the prices and that the drugs should be subjected to continuous performance assessment to as to actually ascertain that they are actually doing what they say on the tin. Reimbursement decisions should be organic and with the list reflecting current priorities. The basic mantra should be: easy entry, easy exit,” he boldly proposes.

Berlin-Chemie Menarini’s country manager, Petras Letauta, echoes this sentiment about obvious shortcomings with the list. “There’s ultimately a lack of consistency in the decision making. In some therapeutic areas, such as in psychiatry, fresh innovations are making it onto the list that are not even available in more established markets like Germany, but in other categories you have the longest waiting times in the whole of Europe. A lot of outdated, classic medicines are reimbursed 100 percent when it would actually make more sense to have a more equitable spread of copayments where you charge something nominal like five to ten percent to the patient and free up some budget to spend on more advanced and effective therapies that are now available,” he suggests.

The authorities, for their part, are swift to recognize these deficiencies and insist that they have clear programs in place to rectify them. “Lithuania still needs to develop its own Health Technology Assessment (HTA) capabilities in order to ensure that the medicines reimbursed are creating the value expected in terms of patients’ life quality and costs of treatment. We started to develop our capabilities on this front in spring of 2017 and we expect to the requisite structures in place by 2019... it takes time to implement because it also needs to be backed up with a proper monitoring system to also follow up on the results after such drug entered to the positive drug list,” confesses Gintautas Barcys, director of the State Medicines Control Agency (SMCA).

“We do accept that there is a limit to the finite public resources we have at our disposal and that we simply cannot reimburse all new medicines coming to the market so there is an urgency in developing new tools to differentiate between products and so that these decisions are calculated objectively and scientifically,” reinforces Jūratė Sabalienė, director of the National Health Insurance Fund (NHIF).

“Right now, levels of reimbursement are determined mainly in accordance to the purpose of the drug: a 100 percent coverage will be reserved for life-saving drugs...
such as certain oncology products while the 80 percent coverage is mainly ascribed to chronic diseases. Then there are two further bands...Clearly we need to refine this system and bring it up to date with current needs and advances in medicinal science. When we are talking about the complexity of an entire healthcare system we obviously can’t copy and paste wholesale from one country to another, so our main objective is to gather the best practices in each country and adapt what is adaptable to the Lithuanian system such as instilling a deeper sense of pharmaco-economics,” further elaborates Sabalienė.

"AS LITHUANIA’S POPULATION CONTINUES TO DECREASE AND AGE, FOSTERING INNOVATION IN THE PUBLIC HEALTHCARE SYSTEM BECOMES A NECESSITY, NOT A LUXURY" 

— Rūta Pumputienė

IFPA’s Leonas Kalėtinas very much agrees. “The existing pharmaco-economic model needs to be further developed by moving from purely cost criteria to an outcome-based system that will ensure that the innovative medicines reimbursed are certainly creating the expected value in terms of better patients’ life quality and lower cost of treatment. We strongly believe that this new approach will help the government to achieve the national healthcare goals in a sustainable but also effective way.” He also acknowledges that one of the main barriers to making this happen is the lack of monitoring, oversight and data collection capabilities. “On one side, we are very glad to see that the Lithuanian government is quite aligned with the development of such a type of reimbursement model. But, on the other side, the country is patently still lacking the health data, processing abilities and methodologies needed to instill an effective value based system,” he warns.

Challenging though it may seem, the country has no option, but to progress down this path, in the opinion of LAWG’s Rūta Pumputienė. “As Lithuania’s population continues to decrease and age, fostering innovation in the public healthcare system becomes a necessity, not a luxury. It’s estimated that in 40 years’ time, healthcare will cost at least two percent of average GDP, therefore policy makers need to focus on innovative treatment methods, which bring better treatment results, shorter treatment durations and greater medicine safety which later helps contain costs and reduce expenditure. There is simply no alternative pathway to averting a crisis and to exiting this crunch point,” she exclaims.

Interestingly Darius Sinkevičius, chairman of the board of the Lithuanian Association of Generic Pharmaceuticals Manufacturers (VGA) and managing director of KRKA, envisages an even more ambitious drug evaluation mechanism. He is calling not only for HTA to be deployed to differentiate between the comparative qualities of novel medicines, but for it to be expanded to take into account the merits of incremental innovation around dosage or drug delivery systems. “In our dialog with the authorities,
Hidden Surprises

market and represent demonstrable improvements compared to existing treatments,” he argues. “The bottom line is that, currently, different stakeholders perceive value in different ways,” explains Mindaugas Plieskis, Janssen’s head of medical affairs for the Baltics. “There is a lack of shared common understanding about what actually constitutes real value when assessing the likely impact of a new therapy. Janssen is very eager to sit down with the authorities, payers and healthcare providers to establish an agreed framework where the value of our overall contribution is properly appreciated. We believe that, as a company, we can simultaneously deliver not only considerable benefit to patients by way of clinical outcomes, but also savings to payers, employers and society at large. Right now, value is being calculated in a very piecemeal fashion, molecule by molecule, whereas we would like to be currently developing a pricing system for fix dose combinations. This type of medicine is the innovation the generic players bring to the market and creates interesting breakthroughs in terms of better patients’ adherence to the treatment and lower cost of treatment,” he recounts. “The current pricing arrangement for these drugs does not enable our members to sustainably market them in Lithuania since the price, by law, has to be the sum of the cheapest price of each ingredient. Yet these are precisely the sorts of medications that can take costs out of the system by delivering up considerable social and economic benefits. We are pushing for a pharma-coeconomic sensibility that takes all of this into account and subjects our incremental innovation to the same sort of future regulatory framework as for innovative medicines, since these products are also unique in the market and represent demonstrable improvements compared to existing treatments,” he argues. “The bottom line is that, currently, different stakeholders perceive value in different ways,” explains Mindaugas Plieskis, Janssen’s head of medical affairs for the Baltics. “There is a lack of shared common understanding about what actually constitutes real value when assessing the likely impact of a new therapy. Janssen is very eager to sit down with the authorities, payers and healthcare providers to establish an agreed framework where the value of our overall contribution is properly appreciated. We believe that, as a company, we can simultaneously deliver not only considerable benefit to patients by way of clinical outcomes, but also savings to payers, employers and society at large. Right now, value is being calculated in a very piecemeal fashion, molecule by molecule, whereas we would like to be

Medtech Mastery

German headquartered medical technology giant B Braun has been present in Lithuania since 1996, growing its revenues by 50 percent since 2007. Although now focusing primarily on the fast-growing out-patient market, Kestutis Liauba, B Braun’s managing director for Lithuania, notes that “the four main divisions of the company are present in Lithuania: hospital care, the out-patient market, B Braun Avitum and Aesculap – the division related to surgical technologies such as instruments, implants and joints.”

Despite a historic lack of government funding, Liauba is reasonably optimistic in terms of the future prospects for the Lithuanian medtech market, pointing out that “over the course of the last few years, the budget for medical devices has been increasing at approximately seven percent on an annual basis. Looking ahead, I am delighted to confirm that in late 2017, Lithuania’s parliament introduced a new state budget for patients of around EUR 1.7 billion; an increase of 11 percent of the total healthcare budget this year.”

Liauba feels that the driving factor behind his affiliate’s success in Lithuania has been the adoption of an integrated total solution approach. He proffers that “For the last three years, we have been implementing the total solution approach in Lithuania – internally, we name it the ‘therapy approach.’ For instance, the ‘infusion therapy approach’ will include the drug itself but also the infusion pumps, its intravenous system and any other part that will ensure the safest treatment for the patients. By offering the complete treatment package to healthcare professionals, patients are benefiting from a cheaper and safer treatment as it is a closed system.”

LITHUANIA MEDTECH

MEDICAL DEVICES EXPORTS

2012 €177M

2014 €180M

MAIN EXPORT COUNTRIES ARE

UK FRANCE RUSSIA SPAIN USA

Source: Life Sciences Baltics, 2016
judged more by our overall contribution to the country,” he stresses.

**GENERICs: FEELING THE PINCH**

Given that Lithuania is subjected to what LAWG’s Rūta Pumputienė describes as, “some of the most exorbitant generic and off-patent medicines in the entirety of Europe,” it is hardly surprising that this particular segment of the pharmaceuticals market has been earmarked for cost containment and price slashing by officials.

In July 2017, the parliament correspondingly approved an amendment of the legal act for reimbursable generic and off-patent drugs in which these medicines are no longer able to hold a price tag ten percent higher than the lowest one in eight reference countries. “The aim of these measures,” explains Pumputienė, “would be not only to reduce co-payment rates, but simultaneously to stimulate price competition among generics manufacturers with a view to lowering reimbursement money on generics.”

Aki Kasvi, general manager for the Baltics at Janssen strikes a similar tone. “These reforms are most definitely a step in the right direction. If you want to ensure that the most innovative products are reaching the market in the proper fashion then expenditure on generics has to be trimmed. This is not a question of discriminating against generics, but rather about rationalizing health spending and leveraging generics in the correct manner as an important part of the toolbox,” he opines.

Meanwhile, the government has also been weighing up the possibility of introducing a so-called ‘cheapest generic substitution’ requirement for pharmacies under which the government would only reimburse the medicines with the lowest price in the market. “We obviously want to ensure fair prices and be sure that the state is always getting value for the money it expends, but equally we strive to foster greater uptake of generics usage and oblige pharmacists to provide the cheapest generic in the market,” reasons Kristina Garuoliene, vice minister of health. “Overall the government strategy is rather balanced, because, although on the one hand, generics producers are being hit with a pretty swingeing haircut, this is happening in combination with an unprecedented push to genericize the marketplace,” observes Valeant’s general manager for the Baltics, Tomas Liesis.

However, the generics industry itself argues that some of these policies may well prove counterproductive. The VGA’s Darius Sinkevičius describes the present state of affairs quite bluntly. “The current pricing pressures that we are under is creating quite a de-alignment between the shares of volume and value that generics account for in the local marketplace... People would do well to remember that the contribution of generics producers is quite significant since they are not merely giving access to high quality treatments at reduced prices, but also freeing up funding that can instead be re-invested into latest-generation innovative therapies, which makes us an important part of the access-to-innovation equation,” he warns.

“Although generics producers are being hit with a pretty swingeing haircut, this is happening in combination with an unprecedented push to genericize the marketplace,” says Tomas Liesis of Valeant.

“In short, the government needs to be wary about just how far they go in terms of slashing our profits, because too high price erosion might actually force up the prices as we could witness pulling their products out and a decreasing number of players present in the market!” concludes Sinkevičius. “We are already seeing some signs of this: Rambaxy vacated the local market because the margins they were making had been so squeezed that it invalidated the business logic,” remarks Berlin-Chemie’s Petras Letauta.

Ominously, the Competition Council is also less than enthusiastic about price caps. “Quite frankly we have some mixed feelings about some of these price reforms,” confides Šarūnas Keserauskas. “While it is clearly commendable that the Ministry is endeavoring to generate better value for each euro expended, they are trying to do this by direct regulation of prices and this is not necessarily sensible. While this will...”
Indeed, force down prices in the short-term, this could well be at the expense of long-term incentives to compete. The danger is that if price caps are too low, they may create drug shortages and reduced quality because only a handful of companies will be able to operate a sustainable business at that level. These good intentions may, therefore, trigger unintended and unwanted consequences. Our advice is that finding ways to incentivize competition under freely functioning market conditions is always going to be preferable to artificial price-setting by the state, which risks distorting the market in a most undesirable way,” he opines.

**WHITHER ACCESS TO INNOVATION?**

Where does all of this leave access to innovation? “A mere 22 percent of all the innovative drugs that were centrally approved by the EMA from 2006 to 2015 reached Lithuanian patients during that period. When you start comparing timeframes, it takes on average 971 days from the point an innovative drug is approved by the EMA for it to reach the Lithuania, whereas, as a benchmark, it generally takes 120 days in our home market of Denmark,” recounts Novo Nordisk’s Valatka.

However there can be little doubt that there have been noticeable improvements in recent months and the general mood amongst industry is optimistic. “If we look back to the low point of 2012, Lithuania was coming in at second from bottom in EU-wide rankings for speed of access to innovative treatments. Today we still lag behind the EU average, but we are now much more aligned with neighboring countries in Central Europe, so these achievements certainly do deserve recognition,” enthuses Raimundas Voishka, Pfizer’s country manager for the Baltics and Belarus.

“Lithuania, like its Baltic neighbors, is becoming more and more open to innovative medicines and this goal has been established as clear priority of the local government. Consequently, while other more mature markets are struggling to offer growth to companies, leading pharma players with innovative added value solutions will find certainly profitable opportunities to market their solutions here,” he continues. “Concretely, at present, innovations are still coming late to the Baltic States, but we can properly sense the improvements underway.”

Janssen’s Aki Kasvi wholeheartedly agrees. “Lithuania is becoming friendlier towards innovation and we have seen some easing up of market access. As a company, we are sympathetic to a government that has to make difficult decisions and we accept that the funds available are limited. There is a pressure from the public to have innovative medicine both available and reimbursed and yet that is juxtaposed with an inability to pay for it so obviously the right balance has to be struck and Janssen is ready and eager to play its part in coming to the table with possible solutions.”

Interestingly the authorities are receptive to such an approach with Kasvi confirming that, “Lithuania distinguishes itself in possessing the appropriate market access tools in place to establish performance based agreements.” Already the country has started to see the
advent of various industry-payer accords and the closure of managed entry agreement deals between MNCs and the NHIF. “I am immensely proud to say that there are over 100 such agreements in force at the moment and practically all of them were signed over the course of the last four years,” reports IFPA’s Leonas Kalėtinas.

“We are already developing some risk sharing agreements with the industry in some key therapeutic areas such as oncology and hepatitis C in which we evaluate the reimbursement of the medicines according to their therapeutic performance,” reasserts vice-minister Garuoliene. “And as we make headway in building up patient registries, I’m sure that this style of operating format will surely become more common in the months and years to come,” she predicts.

A further attribute is the way in which the small Lithuanian market lends itself towards experimentation. “In an ideal world, the Baltics present the sorts of advent of various industry-payer accords and the closure of managed entry agreement deals between MNCs and the NHIF. “I am immensely proud to say that there are over 100 such agreements in force at the moment and practically all of them were signed over the course of the last four years,” reports IFPA’s Leonas Kalėtinas.

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A ROARING CLINICAL TRIALS SPACE

Moreover there are other pull factors that are enticing in MNCs beyond just the meager local market demand. Clinical trial opportunities are one such feature. “When considered on global scale, the weight of the local clinical research segment is fairly slight, but that shouldn’t detract from the fact that research-based players are nonetheless being quite active in this domain with investments running at approximately EUR 35 million per annum. The factors that position Lithuania right at the forefront of the Baltic region in this respect tend to be the existing capacity of clinics as well as rigor of local academia and the well trained and highly professional pool of researchers,” details Kalėtinas. “We certainly invest deeply in clinical research in Lithuania and the other Baltic states and are proud to be positioned as one of the strongest players for this kind of activity,” confirms Pfizer’s Raimundas Voishka. “The main selling points are the exemplary quality of the clinical data and the speediness with which trials can be arranged and executed. These two factors make the country an appealing destination,” he adds.

AstraZeneca, which is also in the top three for conducting clinical research locally, has come to very similar conclusions. “I believe here you can find a good combination of attributes such as speed, quality and reasonable cost all of which are absolutely critical in the success of clinical trials,” analyses Martynas Jocys, the general manager for Lithuania and marketing director for the Baltics. “All the European regulations and practices are properly applied and the costs are very affordable. Moreover, when it comes to the untreated patients’ pool – since in the region the accessibility of medicines is still somewhat limited – we experience good recruitment rates. Finally we find ourselves able to sub-contract to professional and competent CROs in the local marketplace to run the actual trials on our behalf,” he concludes.

Eschewing complacency, however, the Lithuanian authorities are keen to do even better. “We are confident that the clinical research arena presents good opportunities, but are still aware of certain areas of under-development such as the weak collaboration between large hospitals and clinics in the countryside. We are therefore calling upon stakeholders to build up a solid network of clinical trials nationally in concert with our neighbors with a view to creating a hub of excellence for the entire region,” declares the SMCA’s Gintautas Barcys.
When you cast your eyes over the consumer market for a country the size of Lithuania, then there are obvious limitations especially as the population is undergoing further depletion. However these pressures can simultaneously provide impetus for trying things differently and we have seen a lot of evidence of these markets excelling outliers and test beds. Estonia is at the vanguard of pioneering block-chain technology in a healthcare setting. Latvia is too is pressing ahead with tentative initiatives to become a data driven nation in terms of the care process. Here in Lithuania you encounter a radically experimental laser industry that is pushing the technological boundaries, a biotech segment that is increasingly gaining traction, and some interesting trial runs being done on types of risk-sharing models.

His colleague, Mindaugas Plieskis, reinforces this concept. “We are very committed to making maximal use of markets like Lithuania as laboratories to test our innovative approaches and processes, which can then be deployed as showcase examples and exported to other affiliates in more unwieldy, complex contextual environments. Gene mapping or participating in the e-health and digitalization represent contexts where Janssen affiliates in the Baltics could potentially be first movers,” he observes. “As such, we have come to be seen as a benchmark and standard for the rest of EMEA in terms of business development and execution.”

“The three Baltic nations most definitely lie in what you could call the pilot zone,” clarifies EY’s Linas Dičpetris.

“When you cast your eyes over the consumer market for a country the size of Lithuania, then there are obvious limitations especially as the population is undergoing further depletion. However these pressures can simultaneously provide impetus for trying things differently and we have seen a lot of evidence of these markets excelling outliers and test beds. Estonia is at the vanguard of pioneering block-chain technology in a healthcare setting. Latvia is too is pressing ahead with tentative initiatives to become a data driven nation in terms of the care process. Here in Lithuania you encounter a radically experimental laser industry that is pushing the technological boundaries, a biotech segment that is increasingly gaining traction, and some interesting trial runs being done on types of risk-sharing models.”

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**GLOBALIZATION OF THE LITHUANIAN LIFE SCIENCES INDUSTRY**

<table>
<thead>
<tr>
<th>Company</th>
<th>Employees</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>BIOTECHNA</strong></td>
<td>150</td>
<td>Biopharmaceutical company developing and producing two biosimilar drugs</td>
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<tr>
<td><strong>VILTECHMEDA</strong></td>
<td>70</td>
<td>Medtech company developing and manufacturing syringe pumps</td>
</tr>
<tr>
<td><strong>FERMENTAS</strong></td>
<td>350</td>
<td>Biotech restriction enzymes developer &amp; producer operating worldwide</td>
</tr>
<tr>
<td><strong>SANITAS</strong></td>
<td>130</td>
<td>Stock exchange listed generic drugs manufacturer operating in CEE</td>
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</table>

**TEVA**

- 150 employees
- Biopharmaceutical company developing and producing two biosimilar drugs
- Became part of TEVA (Israel)

**MOOG**

- 70 employees
- Medtech company developing and manufacturing syringe pumps
- Was sold to MOOG Medical Devices (US)

**Fermentas**

- 350 employees
- Biotech restriction enzymes developer & producer operating worldwide
- Merged with Thermo Fisher Scientific (US)

**Sanitas**

- 130 employees
- Stock exchange listed generic drugs manufacturer operating in CEE
- Has been acquired by Valeant Pharma (Canada)

Source: Vilnius Biotech, 2017
HCLS: How has the nature of your services evolved over time?
ES: Our workload doesn’t remain constant throughout the year. It’s more a question of peaks and troughs. If the Health Ministry suddenly introduces new legislation or the regulator starts to alter the legal frameworks, then we will suddenly see a spike in activity as pharma companies scramble to align and comply with the new rules of the game. A revised law governing IVF treatment is currently in the process of being formulated, so naturally we are receiving a lot of requests on that front.

I think it’s fair to say that there has been an evolution in demand over time. Initially, when clients were first entering the market, there was a big focus on helping them set up their legal entities. The first decades were all about building businesses from scratch. Nowadays many of these clients have managed to attain well-established local footprints and their needs revolve more around regulatory compliance and high-level services in anti-trust or litigation.

HCLS: What would you say is the typical profile of your clients in the life sciences sector?
ES: In the past, we have assisted heavyweight actors such as Sicor-Teva and BiotechPharma in relation to expanding their construction facilities as well as mentored medical centres such as Northway with regard to navigating the regulatory and tax regimes. We also assisted Canadian company Valeant to acquire pharma unit Sanitas, US company Termo Fischer to acquire local biotech company Fermentas. Currently we are assisting...
our client Euroapotheca in the process of acquisition of the chain of pharmacies in Sweden and hope that this transaction will close successfully. There is long list of other success stories in our pharma chapter. Our client account network is really second to none in this region. We provide legal services to the world’s largest and most innovative pharmaceutical companies, as ranked by Forbes and represent the 8 largest producers of food supplements in the Baltic States, Eastern Europe and the Nordic countries. These are companies that enjoy a combined 70 percent share of the entire Baltic food supplement market. At the same time, we also advise the 4 largest hospitals and healthcare centres in the Baltic region. Our reputation is such that big name brands will often come to us as the first port of call. There are, of course, limitations. Sometimes we will find we are not able to work with a particular company because of conflicts of interest with one or more of our existing clients, but this is very much part and parcel of being a law firm.

**HCLS:** Where do you identify the main competition coming from?  
**ES:** Competition is much fiercer today than in the past and comes from a variety of different angles. First there are the big-brand American or European multinational law firms that sometimes have global client accounts with the major pharmaceutical developers. Often we can coexist harmoniously with them because they don’t have our depth and reach across the Baltics so find it easier to sub-contract specific tasks to us. Another threat comes from the pharma companies themselves when they set up their own in-house legal departments in a bid to keep down costs. Nevertheless, there is still an element of harmonious coexistence. In house departments will generally be able to take care of day-to-day, run of the mill legal functions, but will need to defer to us when it comes to real added-value services that require an insider familiarity with the complexities of the local marketplace.

A further interesting development has been the encroachment of professional services firms into territory initially reserved for the legal profession. We have noticed that companies like EY, Deloitte and PwC are no longer satisfied with delivering audit and tax advisory solutions, but have been pretty aggressive in assembling clusters of lawyers according to market industry segment and have been diversifying and expanding out their service offerings.

**HCLS:** Last year you were awarded ‘Market Maker’ for Lithuania, which means you received acclaim by CEE Legal Matters for your role in creating a modern legal market. What did this award mean to you? And what does it say about TGS Baltic’s abilities to shape the local legal ecosystem?  
**ES:** Receiving this award was a huge honour for me when I think just how far we have come as a nation in fostering a legal ecosystem in line with international norms. TGS Baltic very much does strive to shape the environment that we operate within. A few years ago we played a big part in the design of frameworks to regulate food supplements. Our clients we concerned that the loose regulations that had been in place were inadequate and that supplements, not being treated as pharmaceuticals, were falling through the gap. The solution was to gather together industry and the authorities and to assist them in creating a new legal basis. We would actually like to be doing more in the way of counselling the authorities on the design and revision of life science sector regulations.
LEADERSHIP IN LASERS: A FLASH IN THE PAN OR ENDURING FUTURE?

Unbeknown to many, Lithuania has managed to carve out a niche for itself as one of the world-beaters in the design and production of cutting-edge laser technologies. The country’s original dalliance in this field occurred in the early 1960s, not long after US physicist Theodore Maiman created the first laser, when the Soviet authorities designated Vilnius as an epicenter of state research initiatives in fundamental and applied laser physics. While developing this new direction of scientific enquiry, tunable wavelength picosecond and femtosecond optical parametric amplifiers were created and original ultrafast spectroscopy methods were developed and optimized.

“Laser research started off in labs over here during Soviet times and, after the collapse of the USSR, Lithuanian scientists managed to pick up that baton and run with it… Scientific research, which originated in academia, has subsequently ultimately given way to an impressive number of breakthroughs and important commercial developments, such as OPCPA technology and TW femtosecond lasers that are currently pushing the frontiers of attosecond science,” proudly narrates Petras Balkevičius executive director of the Lithuanian Laser Association.

The eventual blossoming of this homegrown industry has been little short of meteoric. The last five years have been especially impressive registering an almost doubling of sales growth from EUR 46.5 million in 2011 to over EUR 90 million in 2016. Whereas only a decade ago, the entire cluster consisted of a mere handful of entities, today the local industry boasts more than 30 enterprises employing over 800 people, out of which which almost 10 percent possess PhD degrees. Moreover, rapidly growing activities in laser material processing have enabled Lithuanian laser products to reach beyond just the scientific research domain and penetrate the greater industrial market, where, nowadays, nearly a half of total sales are taking place.

What are the factors underpinning such a success? Many commentators speak of a strong cohesion and collaborative streak between R&D activities in laser companies and academic research centers, which confers a certain competitive advantage. “Given the tiny size of our market, it was important that stakeholders joined forces and worked together instead of competing head to head. If you cast your eyes around the local ecosystem you will find that there is very little duplication and instead every start-up has occupied their own little niche whether that be opto-mechanical components, optical coatings, micro-fabrication, short and ultra-short pulse lasers and so on,” reflects Algirdas Juozapavičius, managing director of Light Conversion, a leading manufacturer of tunable wavelength femtosecond laser systems. “This was quite a natural phenomenon in the beginning because we were all spawned from the same couple of academic institutes, but happily this spirit of solidarity and endures today and has served to render Lithuania a

**GROWTH IN LASER SALES**

(MILLION EUR)

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<tr>
<td>Sales</td>
<td>29,4</td>
<td>37,6</td>
<td>46,5</td>
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<td>62,3</td>
<td>70,0</td>
<td>80,1</td>
<td>90,7</td>
</tr>
</tbody>
</table>

Source: Lithuanian Laser Association, 2016
The products of the Lithuanian laser sector are extremely diverse, comprising different lasers, optical, electronic, mechanical laser components, assemblies, parts or combinations thereof to the point where we now can speak of an entire in-country ecosystem... this could surely only have been achieved in such a short space of time through the tight and steadfast collaboration of the researchers in scientific institutions and the engineers of the various enterprises,” agrees Vidmantas Sakalys, CEO of Femtika, a university spinoff dedicated to laser-based precision 3D micro-fabrication.

“It’s the fruit of a great harmonization of energies and efforts.”

Interestingly many of these enterprises are now seeking to apply their technologies to the medical domain. “The original rationale behind establishing Femtika was to create laser micro-fabricated scaffolds for bio-pacemakers that would hold stem cells in place within the heart,” confides Sakalys. Nowadays his company is collaborating with a French entity that is attempting to produce micro-robots capable of entering the human bloodstream, taking diagnostics measurements and exiting again. “By deploying our...
lasers, we can reproduce mechanical structures in micro dimensions half the width of a human hair and capable of fitting on the head of a needle,” reveals Sakalys, though he admits that commercialization of the proposed robotics is “probably still at least five years away.”

Others identify great scope for deploying their creations in slightly less futuristic health environments. EKSMA, a manufacturer and supplier of precision laser components used photonic instruments has joined forces with a South Korean partner to forge a subsidiary called PhotoSana which will start by produce aesthetic dermatology equipment for removing skin pigmentation, moles and tattoos. Juozapavičius, meanwhile, is eyeing up future business lines for Light Conversion in both the ophthalmology and cardiology segments where lasers can be harnessed for precision surgery.

However, “significant barriers to entry remain,” explains Kestutis Jasiunas, CEO of Ekspla, a pioneer in laser optoelectronics and spectroscopy systems. “While we can perhaps envisage a horizon where lasers play a part in the photonic application for artery investigation and mammography, you are unlikely to see many laser companies suddenly morphing into medical device manufacturers because of the onerous regulatory frameworks governing anything related healthcare.”

Indeed companies like custom laser optics outfit, Altechna have even been holding back their engagement with the life sciences industry precisely because of the regulatory complexities and stringencies involved. “It’s fairly common for us to be supplying optical components to companies that build medical devices, and we are happy limiting ourselves to being part of the supply chain in this manner because it doesn’t expose us to any of the traditional regulations associated with the healthcare scene,” accepts the company’s CEO, Per Moller.

“While, theoretically, we could be contributing a lot more in areas like ophthalmologic surgery, you have to remember that healthcare is a very conservative business sector where incumbents are wary of upstarts and outsiders so it will probably take quite a bit of time before you start seeing more intimate levels of engagement across the two disciplines,” sighs Juozapavičius.

Then there are also long-term existential questions around the local industries future leadership prowess. Pessimists point out that Lithuanian laser production risks ultimately being overtaken by China and Germany that enjoy large manufacturing bases that can be leveraged to scale up activity, while others highlight the systemic fragility of the local industry’s yield-driven supply chains.
**HCLS:** Could you please introduce the main activities and operations of Balux to our international audience?

**MARIUS GIEDRAITIS (MG):** Balux is a logistics company fully specialized for temperature-sensitive pharmaceuticals. At the beginning we were only doing cold chain – between two and eight degrees – but now we are also shipping ambient temperature drugs. I want to stress that we are fully committed to offering our services at the highest level of quality and, in this sense, we have set our goal of having 99.5 percent of deliveries without any deviation by 2019. That being said, due to the high temperature-sensitivity of our shipments, this quality goal is a challenge considering the extreme climates in winter and summer in Europe.

In fact, Balux means “Gold dust” in Latin and I believe that this branding strongly reflects our commitment to quality since any small factor alongside our operations is highly valuable for us in order to offer our clients the highest level of service.

**HCLS:** Can you expand on how the company has evolved since its creation?

**MG:** During our initial steps we were not only serving the pharmaceutical industry but also other sectors in order to be able to survive until we got enough pharmaceutical clients’ portfolios to sustainably support our business. However, since the beginning, our ambition was to be fully focused on the pharmaceutical industry and it was not until 2015 when we finally decided to only serve our pharmaceutical customers. To support Balux’s operations in this front, we have a highly educated team that is constantly updating its knowledge around the new pharmaceutical regulations and other industry dynamics beyond Lithuania.

In terms of performance, I am delighted to confirm that the company has been growing on a yearly basis since 2010 reaching its business peak last year with EUR 1.5 million of revenues supported by 22 fleet assets and 35 professionals. But, looking ahead, we expect stronger growth in the upcoming years based on an investment plan that is already being implemented to modernize as well as increase our fleet and expand our team.

**HCLS:** What specific investments have been planned to remain at the forefront of your clients’ needs in terms of operational capabilities?

**MG:** We have already acquired 12 new fleet assets and we expect to purchase 20 additional by 2018. This investment not only aims to expand our fleet but also upgrade and update our current capabilities selling the old trucks – our objective is to acquire twice the number that we sell. So, based on this investment plan, we expect to nearly double our size reaching EUR 2.5 million of turnover in 2018.

**HCLS:** As a niche pharmaceutical distribution player, what is the major challenge that you face when conducting your operations?

**MG:** Our main concern is to keep the temperature of our cargo according to the clients’ specifications. It is important to consider that most of our shipments are innovative medicines and keeping the temperature at the needed level is translated into saving the cargo, which sometimes can be valued up to EUR 5,000,000 per shipment. Minimizing any potential risk – human or mechanic – impacting the temperature of our shipments is crucial for us and, obviously, for our clients.
A PIVOT TOWARDS RECRUITMENT PROCESS OUTSOURCING (RPO)

As the Lithuanian market matures, profound shifts have been taking place in the arena of human resources and how drug developers go about identifying, acquiring and retaining the personnel they require for a new age of medical science. “There are a number of emerging trends underway that are forcing companies to rethink their headhunting processes,” claims Andrius Dauksa, founder of Pharmadrome, a full-cycle, pan-Baltic recruitment consultancy specializing in sourcing talent for the Pharmaceutical, Biotechnology and Medical Device industries.

Another favoured option by many of big MNCs, nowadays, is to go for a sort of halfway house where they rent an entire team of recruiters for a fixed period of time from one or other of the established manpower agencies, such as Alexander Mann solutions or Hudson. “When your needs are more predictable, and you expect ten or more executive hires per year, this style of embedded on-site executive recruitment process outsourcing (RPO) solution can actually make a lot of sense. Many drug developers understand it is inefficient to be undertaking talent sourcing themselves, but being part of a rather conservative, strictly regulated industry where confidentiality is considered highly important, they are nevertheless still more comfortable having the processes taking place under their own roof,” reveals Dauksa.

Other trends can be perceived in the evolving demand for certain types of profile. “Increased emphasis on real word evidence and navigating increasingly stringent regulatory frameworks is forcing many firms to buildup up new capabilities and skill sets: the huge medical reps teams of the past are tending to give way to specialist medical affairs and market access divisions and these need to be staffed with a different calibre of personnel with business acumen and an understanding of pharmaco-economics,” explains Dauksa.

“In the aftermath of the financial crisis, pharma firms started outsourcing a much greater portion of their non-core functions and HR departments were trimmed down. Previously a number of well-known players had experimented with establishing in-house talent acquisition teams, but, in many instances, these were judged to be inefficient,” he says.

In certain cases, the locus of outsourcing has also been displaced. “Previously, it was common for drug developers to commission local CROs and recruiters to source clinical research associates (CRAs) to do the monitoring of in-country clinical trials. Now that that the entire concept of outsourcing has gone mainstream and become much more widespread, you are seeing a tendency for big pharma firms to sign global master agreements with heavyweight multinational CROs like Covance, Parexel and Icon, which go right over the heads of any local actors,” notes Dauksa.
Perhaps emblematic of how a new style of modus operandi is gaining traction within the Baltics, AstraZeneca has downsized the number of medical representatives deployed and has instead been harnessing digital predictive technology and insight sales especially for seasonal product categories such as vaccines.

The breakdown of Pharmadrome’s order book is also quite revealing as to the HR priorities of many pharma firms operative within the region. Some 50 percent of all requested personnel placements constitute commercial roles like sales marketing, key account managers, and product managers. Then 25 percent relates to sourcing medical affairs and market access officers and the remaining quarter comprise highly specialized roles like pharmacovigilance, data analysis or senior exec profiles.

Dauksa is predicting a similar leap in demand for market access professionals to be forthcoming in the medtech sphere. “The rules around medical devices are clearly starting to stiffen, with the advent of more invasive technologies. Hitherto, everything used to be handled by distributors because it was mostly a tender business and the product managers would fill in the forms themselves. However, greater convergence between medtech and pharma regulatory frameworks, and revisions to the legislation are now forcing companies to ramp up their capabilities in this area. Still we they have not yet reached a stage where the volume justifies having someone in house to perform that function full time and there has been a proliferation of boutique consultancies popping up offering assistance and mentoring in these specific competencies.”

HUGE MEDICAL REPS TEAMS OF THE PAST ARE TENDING TO GIVE WAY TO SPECIALIST MEDICAL AFFAIRS AND MARKET ACCESS DIVISIONS

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Perhaps emblematic of how a new style of modus operandi is gaining traction within the Baltics, AstraZeneca has downsized the number of medical representatives deployed and has instead been harnessing digital predictive technology and insight sales especially for seasonal product categories such as vaccines.

The breakdown of Pharmadrome’s order book is also quite revealing as to the HR priorities of many pharma firms operative within the region. Some 50 percent of all requested personnel placements constitute commercial roles like sales marketing, key account managers, and product managers. Then 25 percent relates to sourcing medical affairs and market access officers and the remaining quarter comprise highly specialized roles like pharmacovigilance, data analysis or senior exec profiles.

Dauksa is predicting a similar leap in demand for market access professionals to be forthcoming in the medtech sphere. “The rules around medical devices are clearly starting to stiffen, with the advent of more invasive technologies. Hitherto, everything used to be handled by distributors because it was mostly a tender business and the product managers would fill in the forms themselves. However, greater convergence between medtech and pharma regulatory frameworks, and revisions to the legislation are now forcing companies to ramp up their capabilities in this area. Still we they have not yet reached a stage where the volume justifies having someone in house to perform that function full time and there has been a proliferation of boutique consultancies popping up offering assistance and mentoring in these specific competencies.”

HUMAN RESOURCES
A Reconfigured Business

Andrius Dauksa

PHARMADROME
ew parts of the Lithuanian life sciences space have undergone quite such spectacular transformation as the pharma and medtech distribution business. “Looking back to the 1990s, it used to be that the wholesalers part of the value chain was highly fragmented with around 300 outfits fighting it out for market share. Most of these entities were pretty tiny and would have managed to conclude two or three exclusive distribution agreements with foreign brands. That meant that pharmacies seeking to offer a full panoply of products would simultaneously need to be engaging with thirty or more wholesalers on a daily basis,” remembers Armila’s managing director Remigijus Mielinis.

That said, the pharmacies landscape also used to be radically different. “There were many regulations governing the structure and reach of pharmacies,” he recalls. “All pharmacies were independent because chains were forbidden, the shareholders had to be pharmacists and you couldn’t have two outlets within a radius of 500 metres, all of which resulted in a very splintered, decentralized ecosystem of over 1,500 disparate entities to be negotiating with.”

However, two major events disrupted that original status quo. “Firstly, the 1998 financial crash bankrupted a great many distributors. Western drug manufacturers had been harnessing the Baltics as a bridge into Russia and the wholesalers would act as the middlemen. When the ruble depreciated dramatically in comparison to the dollar, many distributors went out of business and only the stronger performers, like Armila, managed to extricate themselves and survive by rapidly reducing their Russian risk exposure and focusing on the Baltics or pivoting westwards,” he recalls.

The second big disruption was the accession of Lithuania into the EU. “Not only did this momentous event permit consolidation of the retail sector through the legalization of pharmacy chains, but it also subjected wholesalers to much more stringent regulation and oversight with the application of GDP certification resulting in another weeding out of the weaker players,” explains Mielinis, whose firm is nowadays backed by the might of Walgreens Boots Alliance. Indeed, bargaining power is today firmly concentrated at the top with a handful of 6 wholesalers controlling a massive 96% of the market!
LATVIA
### Top 20 Pharma Companies in Latvia by Value (2017)

<table>
<thead>
<tr>
<th>#</th>
<th>CORPORATION</th>
<th>Value EUR</th>
<th>Growth YoY</th>
<th>Market Share</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>ABBVIE</td>
<td>19,389,720</td>
<td>64.96%</td>
<td>5.95%</td>
</tr>
<tr>
<td>2</td>
<td>TEVA</td>
<td>18,823,181</td>
<td>10.48%</td>
<td>5.78%</td>
</tr>
<tr>
<td>3</td>
<td>SANOFI</td>
<td>16,429,917</td>
<td>4.15%</td>
<td>5.04%</td>
</tr>
<tr>
<td>4</td>
<td>GLAXOSMITHKLINE</td>
<td>15,470,634</td>
<td>-5.45%</td>
<td>4.75%</td>
</tr>
<tr>
<td>5</td>
<td>PFIZER</td>
<td>15,299,362</td>
<td>2.96%</td>
<td>4.70%</td>
</tr>
<tr>
<td>6</td>
<td>HOFFMANN-La ROCHE</td>
<td>15,098,156</td>
<td>-4.13%</td>
<td>4.64%</td>
</tr>
<tr>
<td>7</td>
<td>SERVIER</td>
<td>13,528,619</td>
<td>-0.43%</td>
<td>4.15%</td>
</tr>
<tr>
<td>8</td>
<td>KRKA</td>
<td>13,525,187</td>
<td>13.70%</td>
<td>4.15%</td>
</tr>
<tr>
<td>9</td>
<td>BAYER</td>
<td>12,488,844</td>
<td>11.80%</td>
<td>3.83%</td>
</tr>
<tr>
<td>10</td>
<td>BERLIN CHEMIE</td>
<td>12,405,012</td>
<td>10.27%</td>
<td>3.81%</td>
</tr>
<tr>
<td>11</td>
<td>SANDOZ</td>
<td>11,150,593</td>
<td>7.79%</td>
<td>3.42%</td>
</tr>
<tr>
<td>12</td>
<td>NOVARTIS</td>
<td>9,395,782</td>
<td>-9.47%</td>
<td>2.88%</td>
</tr>
<tr>
<td>13</td>
<td>TAKEDA</td>
<td>8,358,857</td>
<td>-1.27%</td>
<td>2.57%</td>
</tr>
<tr>
<td>14</td>
<td>MERCK SHARP &amp; DOHME</td>
<td>8,351,360</td>
<td>-8.88%</td>
<td>2.56%</td>
</tr>
<tr>
<td>15</td>
<td>ASTRAZENECA</td>
<td>7,369,568</td>
<td>-6.78%</td>
<td>2.26%</td>
</tr>
<tr>
<td>16</td>
<td>JOHNSON &amp; JOHNSON</td>
<td>7,292,611</td>
<td>21.90%</td>
<td>2.24%</td>
</tr>
<tr>
<td>17</td>
<td>BOEHRINGER INGELHEIM</td>
<td>6,693,195</td>
<td>16.07%</td>
<td>2.06%</td>
</tr>
<tr>
<td>18</td>
<td>GRINDEKS</td>
<td>6,240,061</td>
<td>-1.53%</td>
<td>1.92%</td>
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<tr>
<td>19</td>
<td>AMGEN EUROPE</td>
<td>5,641,867</td>
<td>-7.99%</td>
<td>1.73%</td>
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<tr>
<td>20</td>
<td>MERCK-SERONO</td>
<td>5,581,085</td>
<td>1.46%</td>
<td>1.71%</td>
</tr>
</tbody>
</table>

Source: SoftDent

### Consumption* of Registered Medicinal Products in Latvia (2016)

<table>
<thead>
<tr>
<th>Category</th>
<th>2016</th>
<th>2016, %</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>MIL. PACKAGES</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OTHER (HERBAL ETC.)</td>
<td>0,62</td>
<td>1,4%</td>
</tr>
<tr>
<td>GENERIC</td>
<td>33,16</td>
<td>75,0%</td>
</tr>
<tr>
<td>BRAND</td>
<td>10,42</td>
<td>23,6%</td>
</tr>
<tr>
<td><strong>MIL. EUR (INCL. VAT)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>OTHER (HERBAL ETC.)</td>
<td>3,76</td>
<td>1%</td>
</tr>
<tr>
<td>GENERIC</td>
<td>155,59</td>
<td>43%</td>
</tr>
<tr>
<td>BRAND</td>
<td>204,32</td>
<td>56%</td>
</tr>
</tbody>
</table>

Source: LIAA; Central Statistical Bureau of Latvia

### Top 3 Exports/Imports Countries in 2016 (%)

<table>
<thead>
<tr>
<th>Exports Countries</th>
<th>Latvia</th>
<th>2016, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>BALTIC STATES</td>
<td>37</td>
<td></td>
</tr>
<tr>
<td>RUSSIA</td>
<td>19</td>
<td></td>
</tr>
<tr>
<td>UZBEKISTAN</td>
<td>6</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Imports Countries</th>
<th>Latvia</th>
<th>2016, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>LITHUANIA</td>
<td>18</td>
<td></td>
</tr>
<tr>
<td>POLAND</td>
<td>13</td>
<td></td>
</tr>
<tr>
<td>GERMANY</td>
<td>11</td>
<td></td>
</tr>
</tbody>
</table>

Source: LIAA; Central Statistical Bureau of Latvia
Health tourism is a growing sector within Latvian tourism and has very high export potential. The numbers of international patients arriving in Latvia have been growing year on year.

FIRST APPOINTMENT: 85%
REPEATED APPOINTMENT: 15%
AVERAGE LENGTH OF STAY: 5 DAYS
INTERNATIONAL PATIENTS: 48,000
TURNOVER IN INDUSTRY: 20 MILL.

LATVIA MORTALITY RATES FOR HEART AND STROKE

<table>
<thead>
<tr>
<th>Disease</th>
<th>Latvia</th>
<th>EU Average</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cardiovascular</td>
<td>18.0</td>
<td>12.7</td>
</tr>
<tr>
<td>Cancer</td>
<td>10.5</td>
<td>7.0</td>
</tr>
<tr>
<td>Other Causes</td>
<td>12.7</td>
<td>9.0</td>
</tr>
<tr>
<td>External Causes</td>
<td>25.7</td>
<td>7.0</td>
</tr>
<tr>
<td>Digestive System</td>
<td>5.0</td>
<td>3.0</td>
</tr>
<tr>
<td>Respiratory</td>
<td>3.0</td>
<td>3.0</td>
</tr>
</tbody>
</table>

Source: OECD, European Observatory on Health Systems 2017

LATVIA EPIDEMIOLOGICAL PROFILE

28,257 DEATHS

- Cardiovascular Diseases: 56%
- Cancer: 21%
- Other Causes: 9%
- External Causes: 7%
- Digestive System: 3%
- Respiratory Diseases: 3%

Source: OECD, European Observatory on Health Systems 2017
Anda Čakša, Latvia’s minister of health since 2016, discusses the reorganization of the Latvian healthcare system to focus on patient needs, the Ministry’s current key priorities, and the main aspects of the flagship health financing bill.

**HCLS**: What have been your main achievements since assuming position as health minister back in 2016?

**ANDA ČAKŠA (AČ):** My main objective was and still is to reorganize the entire healthcare system, orientated primarily on patient needs – the examination process, treatment and also the payment system – activities and measures that improve the accessibility of healthcare services and reimbursable medicines. In 2017, waiting times for healthcare services decreased on average by 25 percent, and 2017 was the first year when the quotas for state-funded healthcare services did not expire. Another good example is the implementation of the ‘green corridor’ (the possibility to receive healthcare services paid from the state budget funds as quickly as possible) for patients with the medically reasonable suspicion of malignancy which we introduced in October 2016. Thus, more than 54,000 cancer patients received faster and more effective diagnosis. The ‘green corridor’ focuses on defining the way in which patients are treated and the algorithms for ensuring they receive the necessary care quickly.

We managed to gain a significant increase in the number of state-funded healthcare services, including the provision of public-paid liver transplantation for adults (until now, such state-funded service was only available to children under the age of 18). Also, the range of state-funded healthcare services is planned to be expanded with the cardiovascular program, ensuring that transcatheter implantation of the aortic valve will now be paid for by the state.

**HCLS**: How would you describe the Ministry’s key priorities right now?

**AČ:** I would highlight further improvement of healthcare service availability adapted to the needs of the patient which means a greater reduction in patient waiting times. To do that we have to ensure sufficient human resources for providing healthcare services for citizens living all across the country. The further development of the e-health system is also one of the main focuses now.

**HCLS**: What are the main aspects of the flagship Health Financing Bill?

**AČ:** The aim of the reform is to create a sustainable healthcare system with a view to improving public health levels. The new system will be fairer and more beneficial for those who live and legally work in Latvia and make social contributions. The main activities to be implemented, in line with healthcare reform, are: the remuneration of medical personnel, attraction of medical personnel to work in regions, improvement of the healthcare quality and patient safety system, improvement in the accessibility of healthcare services and availability of reimbursable medicines and implementation of the new healthcare financing model.
Svens Henkuzens, director of the State Agency of Medicines in Latvia discusses how a nation’s drug regulator can make it an attractive place to do business, combating drug shortages, and ensuring that Latvian patients have sufficient access to treatments.

**HCLS:** What would you say are your main priorities right now?

**SVENS HENKUZENS (SH):** Our mid-term strategy is striving to make Latvia a better place to do business. All public institutions are encouraged to become more customer oriented. We also look for efficiency gains. Brexit is an important third topic. If we look at the UK’s share of products, it is being redistributed. So we are preparing ourselves to take over some procedures from the UK and seize any emerging opportunities. The other side relates to the national market and ensuring that we don’t experience shortages because of the potential supply chain disruptions brought about by the Brexit process. We are compiling information of products that might be at risk. Let’s not forget that the UK is a reference member state and in certain instances it might be a batch release place or a manufacturing site, so there are other criteria that potentially put products at risk due to Brexit. We want to focus on the products that are really at risk of shortages, and not the ones for which we have alternatives.

**HCLS:** How much of a problem are drug shortages? And what are your strategies to minimize this effect?

**SH:** Shortages are becoming more and more of a problem. As an agency, we of course cannot manufacture ourselves, but we can make sure everyone is informed of any likely supply bottlenecks. On the agency website, we have built a function whereby stakeholders can look up the medicines that are experiencing short-term and long-term shortages and look for alternatives that could replace the products in short supply. Since last year, we have been monitoring availability of vaccines, especially those to do with seasonal flu, and when it comes to shortages that pose a real public health risk, we are communicating actively with marketing authorization holders to ascertain if there are alternatives from other member states that we can secure. We can also trigger shortcuts around issues like foreign packaging so that specific products don’t require any translation and can immediately be fast-tracked to market.

**HCLS:** Given that Latvia is a very small market, how do you ensure that you are relevant enough for pharma companies to want to come in and do business?

**SH:** We do have to find ways to increase the appeal of our market so that drug developers consider it worth their while coming in and launching the best products in their portfolios. Otherwise Latvian patients will be excluded from the therapies that they need. Convincing multinationals to go through the hassle of product launches can be a big issue for small markets like us, because the turnover and profit margins that they stand to make are lower. Our bargaining power is always going to be less than for heavyweight markets with sprawling populations that are too big to be ignored.

We want to make sure that in-country product launches are not perceived as a burden. We are talking with the industry how we can make the system more attractive and streamlined. We are committed to reducing national barriers and complexities to launching products and to making our regulatory processes as user friendly as possible without cutting corners or becoming a ‘light touch’ regulator. In short, we want to make Latvia an easy place to do business if you are a pharma company.
ize Matters. One formidable challenge faced by the small Baltic States when endeavoring to respond to national public health needs in a manner that offers value for money is the sheer weakness of bargaining power when interacting with MNCs that can afford to walk away. “You have to remember that realistically we don’t have a great deal to offer in terms of pure market size and volume and that puts us on a bit of a back foot when it comes to sitting around the table and negotiating prices. One has to understand that, sometimes, there is just one company prepared to come in and tackle a specific disease burden and then our hands are tied because we have a moral obligation and duty to attend to the needs of our nation,” sighs Andrejs Pantelejevs, head of bureau at the Latvian Ministry of Health. “We have, however, been thinking creatively about how to get ourselves out of this trap and that is precisely how we came up with the idea of common procurement between the Baltic states. Indeed, other small states are also under consideration too which is why we have already entered into preliminary discussions with Denmark,” he muses.

“The smart way to enhance our clout is clearly to make our volumes bigger, so we have, this year, centralized the purchase of oncology drugs nationally, meaning that we are buying them both for hospitals and outpatients and are seeking to scale up these kinds of initiatives even more ambitiously to cover the pan-Baltic level,” agrees Marina Truhanova, Deputy Head of the Latvian National Health Service. “As far as vaccines are concerned, we are already collaborating with Estonia and Lithuania and there is scope to go even further if we go on to follow the precedent of say ‘Benelux-A’ style cooperation,” she notes.

Meanwhile, there exist many other types of matters in which the Baltic countries are already acting in concert.

“We have secured an agreement with Latvia and Estonia on cooperation in the areas of GMP, GDP and pharmacovigilance inspections and laboratory testing, so that the word of one of our regulatory agencies stands for all, and my nation is presently preparing some new collaboration memorandums with the Dutch and the Italian agencies,” reveals Gintautas Barcys, director of the Lithuanian State Medicines Control Agency (SMCA).

Then there is the concept of common marketing authorization procedures and the so-called ‘Baltic Package.’ “The main idea at the core is that an enterprise that is willing to use all three languages on the packages of human and veterinary medicines they are selling need then just communicate with one of the three agencies,” explains Kristin Raudsepp, director general of the State Agency of Medicines of Estonia. “To save time, money and avoid availability problems, we strongly recommend applicants to use this Baltic package which we have now rendered a very efficient and user friendly procedure,” she encourages. Industry actors, for their part, tend to be broadly supportive of such developments in the expectation that they can result in win-win outcomes for all parties. “Nowadays all three States are part of the EU, which has certainly helped to accelerate regulatory homogenization. As a consequence, firms like mine are increasingly pursuing similar product launch strategies across the entire region, which is good news because it lessens the bureaucratic load and can result in therapies reaching the patient quicker. It’s crystal clear that the 3 governments are proactively striving to be perceived as a block rather than individual countries. In my personal opinion, this approach is actually rather attractive for multinational companies since, individually, each market may pale in significance, but as a group, can still be considered an enticing prospect,” shrewdly posits Raimundas Voishka, Pfizer’s country manager of Baltics and Belarus.
When it comes to public healthcare, Latvia has long been considered a laggard, both within Europe as a whole and even when juxtaposed alongside its two Baltic neighbours. Much of this derives from a chronically undercapitalised public healthcare system. Back in 2015, for instance, the country spent a mere EUR 1,071 per capita on health, thus leaving the country languishing in second place from bottom in EU rankings, surpassed only by Romania, when measured against the other member states. Moreover a meagre 57 percent of Latvian health spending is currently publicly funded (compared to the EU average of 79 percent), with the remaining shortfall paid directly out of pocket by households, thus creating formidable healthcare accessibility barriers for lower income families.
Much of this is set to change, however, as a reform-minded and ambitious government enacts sweeping changes. “Since I became minister in 2016 we have focused on overhauling the entire healthcare system with a view to prioritizing patient needs and enhancing the accessibility of healthcare services and reimbursable medicines,” enthusiastically exclaims Minister of Health, Anda Čakša.

The centrepiece of such efforts is a brand new, shiny Healthcare Financing Bill encompassing a EUR 200 million cash injection and the roll out of a more sustainable healthcare financing model. “We have resolved to raise and allocate additional funding from social contributions, while simultaneously linking the right to receive a full basket of healthcare services with the payment of social contributions,” details Čakša. “From now on the healthcare system will be demarcated into two distinct baskets: a paired-down version comprising a basic minimum amount of state-sponsored medical assistance that will be received by all residents irrespective of the insurance status; and a full basket for insured citizens, which additionally includes items such as doctor’s specialist services, wider diagnostic examinations, medical care at home and much more,” she elaborates.

Such a step has naturally been resoundingly applauded by the pharma industry, which has long been lobbying for a larger envelope of public money to be channelled towards health. “I believe that the situation is becoming decidedly more buoyant. If we take the statistic of healthcare funding in Latvia, there is frankly not much that any institution or government could have done to build a high quality healthcare system with a mere 3.2 percent of the GDP allocated as public expenditure. Lately, we have witnessed policy makers belatedly recognizing this as a serious issue, and now there is a clear message on how the public expenditure for healthcare needs to increase at least to 4 percent of the GDP by 2020 so we staunchly welcome that,” declares Janis Silins, managing board member of the Biofarmaceitisko ražotāju asociācijas Latvijā (BRAL), an association dedicated to supporting the interests of the biopharma sector.

Roche’s general manager, Rauls Velins, is equally congratulatory. “I’m very optimistic indeed. Mandatory health insurance, as stipulated in the Healthcare Financing Bill, is most definitely a step in the right direction in enhancing access to treatment. Many governments talked about this in the past, and finally we now have an administration that has actually dared to do it…still there is much catching up to do. The out of pocket payments ratio remains way too high. 40 percent of Latvian patients lose a substantial part of life savings to medical fees in their old age, simply because the state cannot provide for them and this is obviously unacceptable for a maturing economy and EU member state,” he argues.

Many, though, may be legitimately wondering why it has taken quite so many years for these steps to finally be taken. “We are not a wealthy nation and initially there were other priorities,” explains Valters Bolēvics, executive director of the Association of International Research-based Pharmaceutical Manufacturers (SIFFA). “Safeguarding our national security has been at the top of the government’s agenda and that has meant fulfilling our obligation to pay 2 percent of GDP to NATO. The incumbent administration has also been very keen to show itself as fiscally responsible and to balance the books so they have been keeping a tight grip on the purse strings. You have to remember that in the late 2000s,
If there is one particular standout reform that showcases the material progress that Latvia is making towards reconfiguring its approach to public health, then that is the rollout of a revised national oncology plan. “We’ve certainly seen a burst of new thinking around how to handle cancer with the unveiling of the revised plan last May,” conjectures Merck’s Evija Buksa. “Not only does the new plan provide more funding for innovative oncology products – with prostate, breast and neuro-endocrine cancer treatment drugs now already added to the list of state compensated drugs list – but crucially it also entails increased attentiveness to early diagnostics, which is exactly what companies like ours have been pushing for.”

Most eyebrow-raising of all has been the implementation of the so-called ‘Green Corridor,’ a streamlined pathway to ensure effective and timely diagnosis and treatment of incidence of cancer. “According to the Green Corridor provision, family doctors with a medically reasonable suspicion of malignancy in a patient have to refer this patient for primary diagnostic examinations within 10 working days. If the suspicion of cancer is then confirmed, the family doctor has to request an appointment at a specialized cancer center for a specialist consultation and secondary diagnostic tests within another 10 working days. A first treatment decision has to be taken no later than one month after the first specialist consultation,” details Roche’s Rauls Velins, another fervent promoter of deploying early diagnostics against cancer.

Health Minister Anda Čakša says the reason why the concept has been so effective is because it focuses efforts on the way in which patients are treated and the requisite algorithms for ensuring they receive speedy treatment. “The value is not the ‘green corridor’ per se, but the patient centricity of the entire approach. By seeing the first results, it’s clear that such a model is great for the patient, but also requires significant restructuring about the way healthcare providers undertake their activities,” she observes.

Latvia experienced a severe economic recession in which GDP dropped a full 10 percent. As a nation, we were borrowing on the international markets so as to make up the shortfall and maintain our spending targets and that essentially meant expending money that wasn’t ours. Soon we found ourselves in an unsustainable situation where we needed to pay off creditors and spend more just to maintain the same level of investment in sectors such as healthcare. Naturally, having endured this hardship, Latvians tend to be keen on the idea of fiscal restraint and responsibility and this is reflected in prevailing politics,” he reasons. “We are, however, confident that we now can see the light at the end of the tunnel.”

For its part, industry does certainly appear sympathetic to the government’s financial predicament and the limitations of the state coffers. “The sharp contraction of the economic crisis did scar the country. When you’ve faced so much turbulence, you need to set up a clear vision on how to survive, not just try and spend your way out of it. You need to balance all the aspects of the economy to prevail. The good news is the economy of Latvia is now in shape to grow again, and we do appreciate that the government still has to be financially prudent... We thus present ourselves very much as a willing partner that wishes to contribute to identifying the optimum solutions to the big societal and economic issues of the day,” affirms BRAL’s Janis Silins.

Merck’s Country Manager, Evija Buksa, wholeheartedly agrees. “Industry most definitely can and must bring some solutions to the table and that is why companies like ours are putting themselves forwards as partners and actively engaging
with different stakeholders via the associations. Flexible contracts, performance-related reimbursement and risk sharing are just some of a broad array of mechanisms and tools that can be harnessed to deliver better value to the public health system,” she affirms.

Nevertheless there is still a need to manage expectations because the outcomes of the reforms take time to materialise. “By our own calculations, today’s reforms will have their biggest impact on the pharma industry around the year 2022, so while there’s a lot to be looking forward to, we still have to exhibit a certain degree of patience” astutely counsels SIFFA’s Valters Bolēvs. “The new financing laws will, of course, go some way to readdressing longstanding imbalances, but we also have to remain realistic. There are many competing claims on the new funding from the need to raise doctors’ salaries, to the need to upgrade hospital equipment and to pay for new treatment types... In the long term, market access should improve, but we cannot expect wholesale changes overnight,” he concludes. “Absolutely,” agrees Romualds Ražuks, chairman of the Latvian Parliament’s Public Health Sub-Committee. “Adopting a reform of this magnitude is merely the first step, the difficult part is actually the application... though i am confident that there will be no backsliding and that the enacted measures are more or less irreversible, ultimate success is still going to hinge upon proper implementation.”

“My presumption is that we’re going to have to mollify people’s expectations about witnessing miracles happening in a very short space of time,” agrees Andrejs Pantelejevs, head of bureau at the Ministry of Health. “Now that mandatory social insurance contributions have been hiked up by an extra 1 percent, we have a big task on our hands to manage citizens’ expectations especially as we have upcoming elections in October and the people will surely want to know where this money has gone to by then!”

PUTTING OUT THE WELCOME MAT

In tandem to attempts to belatedly pump more money into the Latvian public health system, the authorities have also been keen to ease the entry of innovative medicines by simplifying the regulatory process and enhancing the ease of doing business for drug developers.

“The curmudgeonly and uncharitable way in which successive administrations have starved our national healthcare system of resources has rendered it disproportionately reliant on private spending in the form of direct out-of-pocket payments with cost-sharing requirements now applied to nearly all services, and it is the poor that bear the brunt of this state failure with over 1 in 4 low-income households facing catastrophic out-of-pocket spending,” he thunders.

Nor is he enamoured with the freshly adopted Health Financing Bill. Though pleased to see extra funding ring-fenced for health, Apinis decries “a woeful lack of financial protection mechanisms for people with low incomes” and frets that “tying healthcare provision to insurance status in such a ham-fisted manner could prove counterproductive and leave the poorest percentile of society, who are more likely to be uninsured, even worse off than before.”

Inequality and the Scourge of Co-payments

Not only is the Latvian health system characterized by serious underfunding, but it is also notorious for yawning disparities in health in relation to socioeconomic status with recent OECD statistics suggesting that life expectancy at age 25 of Latvians with low level of education is a full decade lower than among those with high education. Former Health Minister and president of the Latvian Medical Association, Pēteris Apinis, believes that this is no coincidence and draws attention to what he identifies as “a longstanding deficit of justice right at the very heart” of the public health apparatus.

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“The curmudgeonly and uncharitable way in which successive administrations have starved our national healthcare system of resources has rendered it disproportionately reliant on private spending in the form of direct out-of-pocket payments with cost-sharing requirements now applied to nearly all services, and it is the poor that bear the brunt of this state failure with over 1 in 4 low-income households facing catastrophic out-of-pocket spending,” he thunders.

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to make are that much lower. Our bargaining power is always going to be less than for heavyweight markets with sprawling populations that are too big to be ignored,” acknowledges Svens Henkuzens, Director of the State Agency of Medicines of Latvia (ZVA).

“Unfortunately we see many instances of medicines are being authorized simultaneously in a number of EU member state jurisdictions, but the company deciding not to follow through with a launch here. They tell us that it is a lot of work establishing local partnerships and striking deals with wholesalers and supply chains for not such a favourable return on their investment. Firstly they launch in big population markets like Poland and Romania and only consider us when they go for a second wave of investment later on,” he sighs.

How might this state of affairs practically remedied? “We are in dialogue with the industry about how we can make the system more attractive and streamlined. We are committed to reducing national barriers and complexities to launching products and to making our regulatory processes as user friendly as possible without cutting corners or becoming a light touch regulator... In short, we want to make Latvia an easy place to do business if you are a pharma company,” confirms Henkuzens. He can already point to some quick wins such as the waiving of cumbersome rules concerning the labelling of languages on drug packaging so that, in the future, a sticker with the Latvian translation will suffice; or the forthcoming implementation of a single payment system for administrative fees for market approval as opposed to the prevailing fragmented system of a cascade of different levies.

What innovative drug developers would most like to see, however, is the implementation of proper health technology assessment (HTA) methodologies that would enable them to demonstrate the superior value of their novel therapies and better argue their case for reimbursement. “We are already working hard through platforms like the BRAL and SIFFA to come up with a commonly shared definition of ‘value.’ Right now, the authorities tend to construe value as being all about the impact that a drug or medical device will have on the budget. What we are trying to do is to shift mentalities so that value is instead considered as the overall impact to society. That includes the clinical outcomes of countering a disease, but also additional factors such as whether it brings a patient sufficiently back to health so that he or she can return to the labour force and start being a productive member of society again,” advocates Merck’s Evija Buksa.

“Having a fully functional HTA mechanism is essential if there is to be real progress,” believes Boriss Birmans, the country manager of Santen. “The problem that we perceive is that there is a tendency to think of healthcare as a cost rather than an investment in people, and both the government and the payers seem addicted to the short-term view.” He gives the example of the failure to reimburse preservative-free eye drops even though therapies containing chemical preservatives are known to provoke allergic reactions and, in some instances, even corneal damage.

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when deployed over the long-term against chronic conditions. “We can provide payers with data of our research and development activities, the clinical trials as well as pharma-co-economic statistics if only they have the capabilities in place to process this information,” he affirms.

Little by little, however, the authorities do indeed seem to inching in that direction. “We are refining our techniques for evaluating drugs and services,” discloses Marina Truhanova, deputy head of the National Health Service (NHS). “In the near future, you’re going to see much more intensive application of HTA techniques to ascertain whether a drug or service is entitled to reimbursement or not... and we are even considering incorporating it as part of the agency of pharmaceuticals to grant more independence to the process,” she announces.

A LIFE SCIENCES MARKET WITH UNIQUE FLAVOURS

Despite the many shortcomings of the public health system, the Latvian life sciences market does, nonetheless manage to stand out from the crowd owing to some rather singularly particular characteristics. Firstly, there is the country’s historic legacy as a manufacturing and design hub for fine chemicals and medical preparation dating back to the Soviet era when leading research institutions were established and the sector designated strategic priority status.

“Many of these vestiges of communist time remain highly performing today under private ownership,” remarks Laila Bekmane, project manager of the export division at the Investment and Development Agency of Latvia (LIAA). According to data from the Central Statistical Bureau, Latvia’s chemical industry numbers 198 companies, most of the SMEs, while employment in chemicals and pharmaceuticals stands stable at 4,740 people. “Moreover the country has cultivated strong specialism in niches such as bioorganic chemistry, biopolymer research, virology and

Smaller, Cheaper and Better Lab Instruments

In 1992, Vasily Bankovsky and Svetlana Bankovska – a couple working at the Latvian Institute of Microbiology and Virology – identified a gap in the market for compact desktop laboratory instruments. 26 years later, the company borne of this idea – Biosan – stands as an idiosyncratic but enviable Latvian medtech success story, with a Red Jacket award as one of the best export brands in Latvia and its products now being used in regions as far flung as Japan, South Korea, Singapore, Malaysia and Indonesia.

Vasily Bankovsky explains that the founders “imagined ergonomic and multi-functional devices that scientists could buy for themselves that would help them save space on their desk, time and money.” Being able to create smaller products has been integral to Biosan’s growth, as Bankovsky notes, “We see an increasing willingness and eagerness to receive a smaller and cheaper version of the same medical devices as to fit in personal space. Most of our medical devices are fairly small and we will continue on this front as we have identified it as one of the keys to success.”

Additionally, as both the founders have scientific backgrounds, they were aware of the number of mistakes being made in labs due to sharing medical devices. Therefore, as Bankovsky highlights, Biosan has “focused our efforts on sample preparation to help minimise the number of mistakes during procedures. Mistakes accumulate due to smaller sample volumes used, lack of intermediate temperature control during mixing, and a lack of systems for air deactivation in laboratories during operation.”

Bankovska continues on this point: “we grew out of the Institute of Microbiology and Virology, which was then responsible for the diagnostics of microbial and viral diseases – this is why it is part of our tradition to take care of this segment. In order to be successful in special diagnostics, special instruments are required. Because technology is in constant development, we try to update and adapt accordingly and present our vision as well as our equipment to every market we go.” Biosan’s desire to keep up with the demands of scientists has seen it build up a wide-ranging product portfolio including instruments for sample mixing, centrifugation, thermostating, cell cultivation, boxes for work with DNA, devices for biosafety, thermostatic control, spectrophotometry and fluorometry.
magneto-biology, and counts as one of only 19 countries in the world capable of producing bioreactors,” notes Bekmane.

Then there is the well-established practice of utilising Riga as a bit of an entrepôt to simultaneously conduct business with East and West. “It’s no secret that Roche’s presence here in the 1920 was primarily about leveraging Latvia as back door into the Russia market when in-country operations in Russia were impossible,” explains SIFFA’s Valters Bolēvics, “Latvia straddles the crossroads, so to speak, with a foot in both camps so can take on a certain added geostrategic significance.”

Furthermore the current market dynamics are not at all bad. According to BMI forecasts, the value of the local pharma market, which, in 2017, stood at USD 567 million, is projected to rise to USD 698 million by 2020, while the local medical device market is also on an upward trajectory and predicted to grow at a CAGR of 3.7 percent in local currency terms over the equivalent period.

Nor for that matter are the local macroeconomic conditions anything but rosy. “I’d say we are endowed with a rather welcoming business environment: In 2017, national GDP leapt up 4.5 percent from 2.2 percent the year before and not only do we enjoy the lowest total tax rate for businesses in the Baltic States, but we are also coming in as 3rd for tax competitiveness across the entire OECD,” points out Bekmane.

RIGA: A SELF-STYLED BALTIC METROPOLIS

Even Latvia’s capital city shines out as an amenable host for situating a pan-Baltic headquarters. Not only does Riga rank as 7th on the list of fastest growing European cities by the number of companies with high growth rates, but it also enjoys a heft and depth of transport, logistic and commercial infrastructure that sets it apart from any other Baltic city.

If you’re going to set up a regional office in the Baltics then Riga is the clear winner according to Ainars Kravalis, Wörwag Pharma’s Baltic country manager. “First and foremost there is a logistical dividend to be reaped from being based right in the middle of the Baltics: while it is true that Lithuania boasts a slightly bigger market, had we been located down in Vilnius, then our opportunities to visit and interact with our Estonian customers would have been considerably limited. The same argument applies for distribution and supply chains,” he argues. “Secondly Riga is a much larger, more mature and industrialized capital city than either Vilnius or Tallinn. There are three times as many flight connections to other European capitals and the catchment pool of human
talent is that much better given the concentration of people and, as you can well imagine, this has quite an effect on the ease of doing business. Whether you are seeking to fly in and out potential business partners, move around the three countries yourself or recruit skilled personnel, you are going to find that it is much simpler if you’re located here,” he determines.

“Nor is it lost on investors that Riga possesses a strong manufacturing and life sciences base dating all the way back to Soviet times when 25 percent of all new drugs designed and 1 in 4 medical products fabricated within the Soviet Union actually originated from here in Riga,” reminds Bolèvics. “This means that we are blessed with an excellent scientific technical knowledge platform and technically orientated universities that make the task of sourcing skilled human capital comparatively easy. Of course, the continued presence and high performance of indigenous generics manufacturers such as Grindex and Olainfarm, many of which were originally SOEs that were privatized in the 1990s, also helps to create a spillover affect meaning that we have an abundant labour pool of scientifically astute talent,” he emphasises.

“If we compare Riga to the other Baltic cities, we are the veteran in the pharmaceutical market with big pharmaceutical companies, institutes and universities giving birth to many medical professionals and distributing channels that are already active. Riga also has a certain scale that allows it to hold its own: a venue with such a heritage is naturally attractive to companies and this is why investors traditionally decide to stay here when they come,” concurs Rolando Huapaija-Delgado, project manager of the Investment division at LIAA.

Stem Cell Banking: On the Rise

Stem cell banking is the collection and cryogenic storage of stem cells, often collected from cord blood immediately after the birth of a child. These cells can then be used for replacing damaged cells in the child itself, or indeed its siblings, in later life. Although this niche is relatively new globally – the first private amniotic stem cell bank in the US only opening in 2009 – Latvia, perhaps somewhat surprisingly, stands at its forefront.

Cilmes Šūnu Banka was the first company in Latvia to offer stem cell banking services, having been established in 2004 and subsequently acquired by the Polish group Famicord in 2009. As business development manager Inese Bolmane explains, “our core business today is essentially the collection, coordination, temporary storage and transportation of umbilical cord blood for testing, treatment and harvesting of secreted stem cells.” Although stem cells can be collected from bone marrow throughout a patient’s life as well as from cord blood at birth, Bolmane is keen to foreground the specific benefits of cord blood stem cells. She notes, “Stem cells from cord blood are biologically younger and more flexible that those from bone marrow and thus they provide greater benefits than bone marrow stem cells. Cord blood mesenchymal cells have not been subjected to pathological changes.”

Bolmane outlines the rationale behind stem cell banking thusly: “Stem cells possess unique qualities. Banking affords you the opportunity to use them in the future in the event of a family member being diagnosed with a disease treatable with transplantation. This is the only way to ensure access to a treatment option when it is most needed in your family.”

She continues, “We like to describe the process as rather like taking out an insurance policy. Nobody knows the future and cannot foresee which diseases could potentially affect their family. Nobody hesitates to insure their car or house, but when it comes to de-risking their health, people don’t really tend to register this as being important, despite it obviously being much more important than a car or a house. We are striving hard to change hearts and minds around this subject.”

This shift in mindset is slowly occurring, partly as a result of increased competition in the Latvian stem cell banking market; a market previously dominated by Cilmes Šūnu Banka. Bolmane points out that, “Our competitors are also promoting the concept of stem cell banking and educating both practitioners and the public about this important development in science. This helps us all and society too.”

Looking to the future, Bolmane predicts robust growth for her sector, positing that “the use of stem cells will become ever more significant as medical science advances. Right now, stem cells are used as a routine clinical modality in treatment of approximately 80 different medical conditions – mainly haematopoietic and oncological diseases. Certainly, in the future, further indications for applying stem cells will be revealed, so this is very much a growth industry.”
HCLS: Could you please introduce Merck in Latvia and the strategic significance of the local affiliate?

Evija Buksa (EB): Merck is proud to have been one of the first movers into the Baltics after the disintegration of the Soviet Union. We have actually been present in all three states since as far back as the mid-’90s. While it makes a lot of sense to coordinate the region as a hub when it comes to transversal functions such as logistics, our biopharma business nonetheless still maintains full legal affiliates in Latvia, Lithuania and Estonia.

Here in Latvia, we possess a rich and diversified product portfolio covering each of the therapeutic areas in which Merck is active from oncology to neurodegenerative disease and women’s health. Aside from our traditional portfolio of general medicines covering segments like diabetes and cardiovascular disorders, we also have a strong biopharma presence in niches such as fertility treatment and in countering neurological diseases such as multiple sclerosis.

HCLS: What is your assessment policy reforms pertaining to women’s health?

EB: The National Health Service should be very proud of their efforts to provide a better standard and level of coverage of women’s health. The state fertility program first started back in 2012 and, step-by-step, there has been tangible progress both in reimbursement and in terms of the number of fertility clinics available and the use of electronic tools to manage patients. If, in the beginning, only a third of patients were reimbursed for fertility treatment, nowadays, in half of all cases the state is paying.

IF, IN THE BEGINNING, ONLY A THIRD OF PATIENTS WERE REIMBURSED FOR FERTILITY TREATMENT, NOWADAYS, IN HALF OF ALL CASES THE STATE IS PAYING.

Latvia is actually registering one of the higher increases in the fertility rate across EU member states. According to Eurostat data, the average number of live births per woman in Latvia rose from 1.22 in 2001 to 1.7 by 2016, giving an increase of 0.48 births. Given these demographics and the positive stance of the authorities, we are expecting the local women’s health segment to hold considerable growth potential.

HCLS: What would you say are the star performers within your portfolio in terms of revenue generation, volume and demand?

EB: Actually we have managed to achieve a very nice spread of product lines here in Latvia. The local portfo-
lio is diversified and well balanced between cardiovascular, neurology and fertility and this has the effect of minimizing our risk exposure. If one particular product isn’t performing so well at a particular moment in time, then we other channels of revenue that can easily compensate.

It is a little difficult to predict trends in demand right now because of the uncertain impact of the recent healthcare financing reforms. What I can say is that expectations are currently running very high and the announcement of an additional 200 million euros cash injection into public healthcare is great news for biopharma and latest generation, innovative therapies for which much of the additional budget allocation is earmarked. Any reduction in co-payments and out-of-pocket expenses for innovative medicine is very welcome. This is a big success because the amount of money the state spends on public health is comparatively very low vis-à-vis other EU member states and previously we had seen no real rise in budget allocation for 5 to 6 years. This moment has thus been eagerly awaited.

**HCLS:** When it comes to market access for innovative medicine, how easy is Latvia as a jurisdiction for doing business?

**EB:** Just like with many European economies, Latvia’s health system is overburdened and struggling to remain financially sustainable. The urgency of containing costs makes the task of reimbursing high value, but high price cutting-edge therapies rather tricky. We detect a strong willingness on the part of the authorities, the regulator and payers to bring in the best in class innovative medicine categories, but the bottleneck is primarily financial. Patient access to the best possible treatments will be limited so long as the public health system remains undercapitalized and the ratio of out-of-pocket payments stays high.

**HCLS:** What are your main priorities looking forwards for further developing the business?

**EB:** This is a highly exciting time for Merck as a company. This year, we will be honouring our 350th anniversary and the theme of our celebrations: ‘Always curious – Imagine the next 350 years.’ This strikes right at the heart of what differentiates us from our competitors, namely the fact that we think of the future in terms of generations, not merely 5-year periods.

In terms of managing the local business, we are expecting some forthcoming product launches such as the introduction of a new therapy for multiple sclerosis. Finally, we will be preparing a state of readiness to be able to seize any new opportunities that might arise out of newly approved and soon to be implemented healthcare financing reform.
LOCAL FIXERS & MIDDlemen: HERE TO STAY

The fall of the Soviet Union in the early 1990s is often credited with sparking a flurry of local entrepreneurialism within the newly independent Baltic States. This certainly appears to have been the case in the pharma and medtech domains, where stories abound of local private entities being hastily established to act as on-the-ground partners to MNCs scrambling to place their products on the market for the first time.

Fanex’s owner Victor Shatz gives a good illustrative account of the scene at the time when describing the birth of his company. “The immediate aftermath of communism was highly disruptive. As a direct result of the intense economic and political changes sweeping the country, the budget of the state owned laboratory I was heading up shrank down to nearly zero, and the average salary of our technicians was reduced to the equivalent of 30 USD per month, so I started to look for partners for cooperation abroad, I sent many letters to foreign companies, with whom we had cooperated before. We were, frankly, willing to do pretty much anything for any Western partner just to keep afloat. Soon, we received a phone call from the head of Millipore Finland, saying that he was actively looking for local partners and insiders, and we were nominated to compete against other two candidates for the distribution function. Though we were familiar with their technology, we had little experience of the distribution business and effectively had to learn on the job. In the beginning, we had a small company within the laboratory, and then later on we rebranded it and developed into Fanex as you know it today,” he recalls.

While large pharma multinationals may have initially resorted to such mechanisms to establish a first footing, it was surely only going to be a matter of time before they would feel confident enough to short circuit the import-distribution service model and establish their own local offices. According to Janis Poritis, general manager of IQVIA for the Baltics, this traditional sequence of events, however, didn’t always hold true. “Actually, in the smaller markets of Latvia and Estonia we saw quite a number of foreign outfits coming in, experimenting with an in-country affiliate and then pulling out again and reverting back to the original wholesaler model and conducting the business remotely using local partners as proxies... MSD was, obviously, the most high profile example of this and it wasn’t necessarily even the 2008 financial crisis that caused these companies to draw in their horns, but rather the realisation that this region’s population is diminishing, drug development is getting more expensive and that it’s difficult to remain sustainable when you’re sinking resources into so many fringe and marginal destinations like the Baltics without reaping an obvious reward.”

Others are not so sure, and insist that representative offices on the ground are the only way to go for any self-respecting pharma MNC. “There was never any question of pulling out and letting third parties represent us,” exclaims Wörwag Pharma’s Baltic Country Manager, Ainars Kravalis. “We were very conscious of the need to maintain a real footprint ... Quite a few multinationals were indeed hasty to exit the market, but found out, often to their cost, that the short-term gains derived rarely outweighed long-term risks of relying upon local wholesalers to be your brand ambassadors. At a first glance, it may have seemed appealing to some foreign investors to reduce overheads by transferring activities over to a local wholesaler and paying discounts, but there are definite drawbacks to entrusting...
your brand to a partner who works with a hundred other companies and cannot devote the level attention to your products that they really deserve. As such, I think there are multiple instances of well-known MNCs, including even heavyweight actors like MSD, misreading the local market dynamics of how to best do business here in the Baltics,” he affirms.

In the medtech segment, meanwhile, far from being a flash-in-the-pan arrangement, the commissioning of local representative partners certainly appears to have held firm. Fanex’s Shatz sheds some light on why that might be the case. “The size of the Baltic market does not justify for most our suppliers to maintain a permanent office. Some major manufacturers of pharmaceuticals do, of course, maintain an embedded local footprint, but the market for medicines is much larger than that for equipment. As long as equipment manufacturers like Waters enjoy a nice market share, obtained via distributors, I do not see serious reasons for them to take this step. For most of our partners is simply too risky to enter a country where they are not familiar with the local habits, not just the language, but the business, research and historical context. To build up that familiarization and local insights takes sustained investment and perseverance and cannot just be created overnight. For most MNCs the tiny Baltics markets don’t justify the time, effort or expense. There would, at best, be an opportunity loss where they could have been generating a bigger bang for their efforts by focusing their energies elsewhere. As such, they instead prefer to entrust distribution to insiders and to alleviate themselves of the hassle they would otherwise have to put up with. I believe that it’s fair to say that the current business arrangement of deploying local partners like us is an enduring, stable and sustainable one,” he reasons.

Giedrius Sprindys of the esteemed Lithuanian importer of orthopaedics, Biomedika very much agrees. “You might think that’s we’d be worried about becoming a victim of our own success and our suppliers becoming emboldened enough to try to go it alone by going direct and cutting us out as middlemen, but actually the population size of the Baltics mitigates against this. Normally the rule of thumb is you need a population of around 10 million inhabitants to be assured of making a direct-to-market model work. The entire region has only 6 million and that’s not even talking about the national markets! If anything, we’ll see more of this type of partnership as multinational small and mid-cap technology providers start aspire to interact with Baltic consumers and as the due diligence capabilities for identifying the right local partner become more rigorous and reliable,” he laughs.

That’s not to imply that local middlemen don’t face challenges however. “We have a new diabetes care product called Libris, which we are still waiting to see delivered up to our market. We hope market access is coming soon, but since our market is so very small the decision actually depends on external factors. Unfortunately there are some complications from a geopolitical perspective because our client, Abbott, wants to be launching this particular product simultaneously in the Baltics and Russia and the registration in Russia is stalled right now as a result of the on-going fallout relating to the Ukrainian crisis. These sorts of hurdles are hazards of the trade when you are an importer in a small, marginal market of limited significance on the grand scale. The partners that you work with may be sluggish to launch their latest generation products in your territorial area, not because they don’t have confidence in your work, but simply because they have greater priorities elsewhere in more lucrative markets so you end up finding ourselves at the back of the queue,” laments Janis Biezbardis, chairman and owner of medical diagnostics importer and supplier, Farmeko.

There are other fears too. “Being a distributor can be somewhat hazardous, because you are stuck in the middle and, if something happens to one of your key suppliers, in our case Zimmer Biomet, say, for example, if they were suddenly acquired and the new owners don’t want to continue the relationship, then you could find your business disappears almost overnight,” postulates Sprindys. “That is why it is essential to diversify out and hedge risk exposure such as we have been doing with our hearing aids business arm which sits alongside the orthopaedic devices and joint replacement technologies,” he adds.
The lack of market data in the Baltics is severely hindering the operations of pharma MNCs, as Ainars Kravalis, Baltic country manager at Wörwag Pharma, laments. “Trying to work out market dynamics in the Baltics can be a bit like trying to peer through a fog because market data tends to be incomplete, fragmented and unstructured,” he notes. “There is no single, reliable data source to go to operating on a pan-Baltic level. For certain parts of the market you have data black spots, whereas in others there are wide discrepancies between the statistics and projections of different providers. This means there is an element of guesswork and needing to read in between the lines. Often MNCs newly entering the market will make mistakes in their calculations,” suggests Kravalis.

In Lithuania, Marijus Valatka, general manager of global diabetes treatment leader Novo Nordisk bemoans the fact that “we do not have a national diabetes registry and every hospital has their own certain kind of diabetes database without any interconnection between them. In our case, this creates major complications to introducing our innovative but also highly needed drugs in the Lithuanian market since it is quite challenging to evaluate their effectiveness locally.”

IQVIA, formerly QuintilesIMS, one of the world’s largest health data providers, does not have a footprint across the Baltics region commensurate with its global leadership position, especially in the smaller Latvian and Estonian markets. Janis Poritis, IQVIA’s country manager Baltics admits that “quite frankly, historically IMS Health didn’t maintain too much of a presence in Latvia and Estonia, because the markets were so small and marginal that it wasn’t deemed commercially interesting. The focus on data compilation was, naturally, much greater in Poland and Lithuania, because of the size of the markets and the number of companies present and thus the greater likelihood of being able to ultimately sell that data.”

Poritis does point out that “Quintiles’ pan-Baltics engagement has been much deeper because this is a decent clinical trials destination region” but notes that “Despite the merger at the global level two years ago, the integration process is still underway over here ... we are still a little way off being able to establish a pan-Baltic situational awareness mapping using real world up-to-date data, of the style you might encounter in many of the weightier, high-performance markets around Europe.”

The highly fragmented health data across the region has provided an opportunity for local service providers to step in and provide the much-needed market data that multinationals could not. Rytis Naginevičius, director of SoftDent, explains, “I identified that the accuracy of pharmaceutical market
analysis in the Baltics was far from reliable because it was based on extrapolations from only 55 pharmacies. Thus, I developed a new method incorporating secondary sales data ... gathering data from national sick funds, pharmacies, wholesalers and hospitals. Since then, SoftDent has been positioned as the leading company for pharmaceutical market analysis in the Baltic region. Companies need reliable sources of market intelligence and, considering that SoftDent has the Baltics’ largest and most diverse healthcare database, we are increasingly able to plug some of those gaps and provide that.”

SoftDent’s solutions are helping state actors as well as private companies. Lithuania has been working to implement an electronic health (e-health) system, but data fragmentation has been restricting its progress. As Naginevičius notes, “One major challenge negatively impacting e-Health’s smooth implementation is the very fragmented data in different hospitals, the variety of systems used in the healthcare points in the country that do not allow interconnection between them, and the low convenience of the current e-Health system in terms of usage. Foxus®, our e-Health solution that enables the storage of patient and medical chart data in an electronic format, would be able to solve most of the challenges ensuring not only accurate information about the drugs but also the value that such medicines bring to society in terms of financial savings and better quality of life for patients with very user-friendly software for doctors.” Naginevičius continues, “Indeed, we have been proposing to the Minister of Health connecting SoftDent with the public data system to check out the feasibility of implementing Foxus® and the benefits that it would create in terms of more transparency and better digital capabilities.”

This region-wide push for greater digitalization is encountering significantly greater hurdles in Lithuania than in Estonia. Vytautas Baublys, CEO of Softneta, an award-winning Lithuanian IT company providing software-based specialized healthcare solutions which has been involved in setting up a medical archive system for the country, points out that “Estonia has only 60 hospitals for its 1.2 million population, including two very big ones. In Lithuania, we have 160 big hospitals [for a 2.8 million population] and each of these 160 hospitals needed to have isolated data and be able to exchange data within seconds.”

Baublys proudly exclaims that Softneta has already been successful in creating savings for the Lithuanian healthcare system, noting that “we believe that we saved around EUR 12 million for the Vilnius University Hospital Santariskiu klinikos.” With sales in over 39 countries, Baublys outlines the company’s unique approach: “We try to be the global solution. Softneta even provides free of charge services. We might be small, but we are very ambitious and our vision is to create a huge market and infrastructure such as that of Skype which could generate the infrastructure necessary for brave and promising scientists to implement the ideas of the medicine processes ... All of our solutions are first trying to solve the problem of data being accessible immediately.”

“ESTONIA HAS ONLY 60 HOSPITALS FOR ITS 1.2 MILLION POPULATION, INCLUDING TWO VERY BIG ONES. IN LITHUANIA, WE HAVE 160 BIG HOSPITALS” — Vytautas Baublys, SOFNETA

HEALTH DATA
Imperfect Visibility

RYTIS NAGINEVIČIUS
director, Softdent
VYTAUTAS BAUBLYS
CEO, Softneta
Can you please talk our readers through Teva’s relationship with the Baltics?

JANIS MEIKSANS (JM):

Teva started its operations in the region through distribution agreements. Today, especially after Teva’s acquisition of the Cephalon / Mepha company, we saw an exponential growth mainly due to Teva’s bold inorganic moves. As far as the Baltic region is concerned, the real game changer was the acquisition of the production site in Vilnius, as Teva does not have many production sites of biologics in Europe apart from the German and the Lithuanian facilities. It puts us somewhat under the spotlight, given that we do not have a biologics production site either in the US or in Israel, Teva’s headquarters.

In short, from being a distribution and marketing organization in the region we became one of the largest producers. This, in turn, had a positive impact on our relationship with the government: now we are considered to be the goodies! Our exports account for about USD 200 million, which, although by international standards is not an especially significant figure, it is meaningful compared to the overall size of the Latvian economy.

How would you describe the strategic importance of the Baltics activities relative to the rest of Teva’s operations in Europe and globally?

JM: At Teva we are a part of a large CEE Cluster which is built of 8 markets and is an important region for Teva European business in terms of scale, population of patients and business efficiency. In smaller markets you have to think twice of how to get things done in an effective way, which is a very valuable experience. This is why I am a strong advocate of the ‘clusterization’ of countries.

One thing we are particularly good at in the Baltic region is sharing functions across borders, taking into consideration that we have three completely different national languages. This is for instance an issue when it comes to packaging as we need to decide whether providing packages in the three national languages and/or using a fourth common one.

I think we can rightly be held as an example as we successfully managed to collaborate in small countries and find common ground. If these paths are followed, the single countries are winning, the clusters are winning, and the companies are ultimately winning, too.

IN SMALLER MARKETS YOU HAVE TO THINK TWICE OF HOW TO GET THINGS DONE IN AN EFFECTIVE WAY

We understand that there has been a repositioning to making Latvia the lead office in the Baltics. How do the three Teva branches collaborate with one other?

JM: If we look at Teva Baltics from a legal perspective, we have a limited liability company in Lithuania and two affiliates in Latvia and Estonia. Based on my experience, I believe that it is of vital importance where you put your talents, and, to this purpose, we decided that we were not going to have one single headquarter in the Baltics. Instead, we have an in-built flexibility which allows us to use are entire catchment area for sourcing talents whenever we have a vacancy for a specific role in one of the three affiliates.

Janis Meiksans, general manager at Teva Baltics, unveils how a cluster-driven model can unlock substantial efficiency gains across small-scale markets.
TOWARDS PERSONALIZED MEDICINE AND A ‘SUPER-LAB’!

Rauls Velins, Roche’s general manager for Latvia, describes his company’s role in helping the Baltic start re-conceptualize how to combat cancer

**HCLS:** Could you please start by introducing Roche in Latvia and the strategic significance of the local affiliate?

**RAULS VELINS (RV):** Roche’s presence in Latvia dates back a long time and we continue to view this country as a very sustainable and prospective market to be engaging with. After the company was forced out of St. Petersburg by the nationalizations of 1918, the strategic decision was taken in the early 1920s to establish an affiliate in Riga essentially as a back-door route for continuing to export into Russia. With business thriving, what had initially been purely a sales and marketing office was subsequently upgraded to include an in-country scientific laboratory and production site. Roche had sustainable growth until September 1940.

Unfortunately, in 1940, we had to vacate the market as Latvia was subsumed into the Soviet Union and private businesses were confiscated and expropriated by the state. However, we returned in 1993 following the restoration of Latvian independence and the reintroduction of an operating environment where it was possible to do business. Interestingly, this year, we will be returning to the historic property on Miera Street that we used to own in the 1930s. Our plan is to unite our pharma business and diagnostics operations under a single roof on these premises.

**HCLS:** How do you perceive the local business winds?

**RV:** The dynamics of the local market are much brighter than they have been in recent years when Latvia was still recovering from a severe economic crisis. That means that investment confidence is on the rise and the outlook is fairly favorable. Even the financial instability of Banks of Non-Residents hasn’t influenced the Fitch Index of Latvia.

**HCLS:** Last Spring, Latvia launched a National Cancer Plan. As a leading vendor of oncological drugs, what was Roche’s involvement in facilitating this endeavor?

**RV:** In 2015, the Ministry of Health announced that they would be holding a campaign called “Oncology Awareness Year” to focus attention on the threat of cancer and, from an industry standpoint, this provided us with an opportunity to advance ideas that could radically improve the predicament of cancer patients. During 2015 and 2016, patient organizations collected more than 10,000 signatures to raise funding for oncology patients and submitted them to the Parliament. We facilitated the visit of Mr. Bergstrom, director of EFPIA, to the MoH. The visit resulted in a common letter that stated the need to increase funding for oncology medicines. Four working groups were established. Roche employees together with other companies are involved in all four groups.
The Ministry of Health subsequently announced oncolgy as its priority, which was vital. As a company, we are satisfied with a number of the showcase achievements of the prevailing oncology plan such as the implementation of the “green corridor”. Equally important, is having an appropriate infrastructure to back up such actions and that means the existence of a “super laboratory” which is another area where we are noticing palpmable progress. A super lab acts, naturally, as the first step into personalized healthcare.

**HCLS:** Presumably this is precisely why Roche has been at the forefront of plans to establish a state-of-the-art pathology laboratory in Riga dedicated to oncology and the principle of preventive diagnostics?

**RV:** That is absolutely correct. When Latvia assumed the rotating presidency of the Council of the European Union in the first half of 2015, Roche invited a delegation to our global headquarters in Basel. Once there, the delegation presented 4 concept ideas for scientific purposes, which our own in-house R&D division agreed to study in depth and develop further. One idea that came out of these exercises and was actually discussed in person at a meeting between the then Minister of Health and Roche CEO, Dr. Severin Schwan, was the proposal of a state-of-the-art laboratory dedicated to differential diagnosis in oncology.

The rationale was principally to create a lab of such a size, scale and elite technology that it would be regarded as best in class across the entire region. Instead of five regular sized labs this ‘super lab’ would become a hive of activity and magnet of expertise in oncology drawing in regional patients. Moreover the focus would be on early diagnostics, precision medicine and personalized treatment of cancer patients. The great news is that this vision is now in the process of becoming a reality. The project has been costed at EUR 5-8 million with EUR 1 million already budgeted for first phase implementation later this year. Everything will go through a National tendering process so we don’t yet know what will be the extent of our own participation, but we are very proud to have contributed to the initial conception of the idea.

**HCLS:** The industry is moving from a ‘one-size-fits-all’ philosophy of drug treatment to a much more personalized approach involving biomarker-based diagnosis and significant differentiation within a single disease. How ready is Latvia to embrace such steps?

**RV:** Latvia is increasingly ready to make this step and the super lab is proof of how seriously the authorities are taking the principles of precision diagnosis and personalized treatment pathways. Right now, Roche is in the process of rolling out our Foundation Medicine (FMI) services across Europe. What that actually means is that we will be assisting oncologists to choose the best individual cancer treatment based on a patient’s unique tumor mutation profile.

As a company, we now have the capabilities to determine cancer driving mutations through next-generation sequencing of a patient’s tumor biopsy and comparing that mutation profile with 125,000 anonymized tumor profiles currently stored in our proprietary tumor profile database. Moreover, the information is grounded in self-learning algorithms that analyze cancer drivers, affected pathways, results from ongoing clinical trials and drugs that have helped patients with comparable genomic contexts.

Crucially this new lab will be able to support our FMI services and that can potentially have a dramatic impact on rendering Latvian cancer treatments more effective and efficient. Right now, our calculations are that, with more precise diagnosis, some 70 percent of cancer treatments given to patients might become more effective. One could conclude that we might significantly improve clinical outcomes and reduce wastage of public money. Rectifying this scenario will be a massive step forward. This might change HC landscape as tumor treatment will not be based on localization but Cancer Gene mutations. ☺️
ONCOLOGY
New Departures

VIROTHERAPY: RETHINKING THE WAR ON CANCER

One thoroughly fascinating medical breakthrough to have come out of Latvia that has been causing quite a stir has been the appearance of Rigvir®, the world’s first and only non-genetically modified cancer virotherapy agent. While virotherapy is only now emerging as a new wave of oncological therapies, Rigvir® has actually been undergoing development for more than 50 years, much of that time under the cloak of secrecy of Soviet labs, and stands as the singular life-long work of a renowned Latvian scientist, Aina Muceniece.

“While virotherapy as a mechanism for cancer treatment has been on the agenda of scientists for many decades, the issue of identifying the virus was always the main stumbling block. The idea of a virus penetrating and infecting cells was obviously familiar to doctors, but the hurdle was more about finding a safe formula for harnessing it,” explains Karlis Urbans, head of business development of Rigvir Holding Company.

His company has surmounted this conundrum by bridling a live non-pathogenic orphan virus identified in small kids, ECHO-7, that has subsequently been adapted for melanoma, but not genetically modified. As of now, there are only 3 registered oncolytic viruses in the world: The first one is Rigvir® which was approved in its home market back in 2004, another, called Oncorine, is registered in China, and the third and most recent constitutes Amgen’s FDA-approved T-vec.

How, then, does it work? “Once Rigvir® finds and selectively infects tumor cells, the virus then replicates within those tumor cells, effectively destroying them,” claims Urbans. “Both of these processes – oncotropism and oncolysis – are selective for tumor cells and healthy cells are only minimally affected, if at all,” he adds.

“Rigvir® finds and selectively infects tumor cells, the virus then replicates within those tumor cells, effectively destroying them” — Aina Muceniece

If, as suggested, the therapy proves effective over time, such a process looks set to thoroughly disrupt conventional practices for treating cancer. “We noticed that whenever pharmaceutical companies address the issue of melanoma, they tend to take into consideration the very late stage of the disease because to some extent it is easier to commercialize their treatments. When life is at stake, there is pressure on behalf of the government to reimburse such medicines... Rigvir®, instead, can also be used at the earliest stage to prevent of the metastasis. It is known that cancer is not curable. However, we learnt that, thanks to our virus, patients have four to six times higher possibility to survive if it is used in early stages,” proudly declares Urbans.

The outstanding obstacle, however, lies in putting together the requisite dossiers and trial data to satisfy the EMA, which considers the Soviet-spec development evidence invalid with the result that Rigvir® is currently limited to the three jurisdictions of Latvia, Armenia and Georgia. “The objective is very much to commercialize the product across Europe, but we accept it will take some time to jump through the necessary regulatory hoops to secure approval,” he candidly acknowledges.
**THE RIGVIR® EFFECT!**

A social partner for Latvia! This is how Kristine Juckovica, executive director, describes Rigvir Holding, the home grown enterprise that came up with the highly disruptive and innovative homonymous virus-based cancer treatment produced by ECHO-7 virus.

**HCLS:** Can you please introduce the structure of the company to our international readers?  
**KRISTINE JUCKOVICA (RJ):** Rigvir Holdings acts as the parent company and is mostly responsible for the marketing, R&D, the business development and the promotion of Rigvir®. The other fully owned company, Latima, is a producer and manufacturing entity as well as the holder of marketing authorization. Latima runs laboratories and it also subcontracts bottling, which is performed in Estonia. Furthermore, we possess a clinic in Jurmala- Global Virotherapy cancer clinic, and center of excellence purely dedicated to treatment.

**HCLS:** Why were Georgia and Armenia chosen as the only two other jurisdictions in which you registered the product?  
**RJ:** Georgia and Armenia are part of the same reality when it comes to accepting clinical trial data that was conducted within the former Soviet Union. The clinical trials that we used as the basis for registration in Latvia would, frankly, not be accepted anymore for centralized registration of oncology medicine. We see the clinical need for this treatment across the world, so are catering to it the best we can. In fact, we receive a fairly large volume of medical tourism to our clinics, mostly from English speaking countries such as the US, the UK, Australia and South Africa.

**HCLS:** What have been your top priorities since assuming the position of executive director?  
**RJ:** My top priority has been about corroborating our current marketing strategy by taking part in conferences and rendering ourselves known to the world. The main bottleneck at the moment is the fact that people do not necessarily know about the disruptive technologies that we use and some of them do not even believe in them. It is, therefore, critical to build up the necessary credibility.

**HCLS:** You seem to be facing a bit of a backlash from multinational pharmaceutical players that feel threatened by your disruptive business model. How do you go about confronting that?  
**RJ:** I think it is safe to say that we are Latvia’s social partner, because we are carrying out a lot of explanatory work of early diagnoses and also calculate that we are able to generate public healthcare savings of about 25 percent of health costs for melanoma treatment. We are not facing a lot of competition per se, but there are a lot of negative advertisements peddled by parties who seek to undermine our credibility. However, we do get some encouragement too. The Latvian Ministry of Health and local FDA have been helpful and so too the national investment promotion agency. Moreover the European Commission has even demonstrated its interest in and support for our work by awarding us grant monies and including us as part of the 2020 horizon framework.

In 2017, we received thorough EMA scientific advice, which is helping us build a roadmap to commercialize our product across rest of Europe. While we are filling the gaps, the path will, no doubt, be long and rocky with many barriers in the way.

**Quote:** WE SEE THE CLINICAL NEED FOR THIS TREATMENT ACROSS THE WORLD, SO ARE CATERING TO IT THE BEST WE CAN.

---

Kristine Juckovica  
RIGVIR HOLDINGS  

**www.pharmaboardroom.com**  
Healthcare & Life Sciences Review: The Baltics
SNAPSHOT IN FIGURES

Estonia

TOP 20 PHARMA COMPANIES IN ESTONIA BY VALUE (2017)

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Source: SoftDent

ESTONIA: 100% OF GOVERNMENT DATA ON BLOCKCHAIN

PUBLIC SECTOR

- POPULATION REGISTER
- HEALTH INSURANCE REGISTER
- VEHICLE REGISTER
- DOCUMENT RECORD MANAGEMENT SYSTEMS
- DOCUMENTS REPOSITORY

PRIVATE SECTOR

- ENERGY
- TELECOM
- BANKS

Source: Republic of Estonia Government

ESTONIA EPIDEMIOLOGICAL PROFILE

15,489 DEATHS

- CARDIOVASCULAR DISEASES: 52%
- CANCER: 23%
- OTHER CAUSES: 8%
- DIGESTIVE SYSTEM: 8%
- EXTERNAL CAUSES: 6%
- RESPIRATORY DISEASES: 3%

Source: OECD, European Observatory on Health Systems 2017
Ain Aaviksoo, ex-deputy secretary general for e-services and innovation at the Estonian Ministry of Social Affairs, explains how digitalization facilitates both economic growth and better services for patients.

**HCLS:** What are the main tasks of the deputy-secretary general for e-services and innovation?  
**AIN AAVIKSOO (AA):** My mandate is to make the best possible use of technology towards innovation, a type of innovation which is citizen-centric. Digitalization facilitates economic growth and if Estonia has a competitive advantage in a certain area, then it is digital data usage, including in healthcare. I am trying to shape the mindset of the Ministry and sometimes I call myself a ‘trouble maker’, because it is an interesting yet a very challenging mission.

**HCLS:** E-health is described as an enabler of access to medicines for Estonian patients. To what extent can digitalization offer solutions to patients?  
**AI:** It facilitates to access every service, not just medicines. What we have created here today is not only solid infrastructure, but also a legal framework, culture and implementation of health services which are all using digital technologies and, more importantly, the cornerstone is here ‘integration’. What we have been actively working on is an ever closer integration of primary and secondary care. We introduced e-prescriptions, for instance, in 2010 and it took us eight months to have it fully implemented, compared to other places like Denmark and Catalonia where the process lasted much longer. The same results can be replicated and implemented anywhere else.

E-prescription enabled us to see whether people actually do buy the medicines that they are prescribed. Furthermore, doctors were mandated to prescribe the medicine by their active ingredient and not by their brand name, to allow patients to discuss cheaper alternatives of the same active ingredient with their pharmacists. We were able to go from 45 percent to 83 percent of generics consumption in three years’ time.

Four years later, we introduced an additional decision-support service that allows doctors to make notice of contra-indications of medicines. In addition to that, this year we are opening up a health information system which was built in 2007 for medical service providers to have access and share patients’ data between themselves. A start-up is piloting this project and is actively working on opening up the service and the data collected by the public healthcare system through mobile devices. This is possible because all Estonians have digital IDs and most of them use them via their mobile phone.

**HCLS:** What is your proudest achievement during your time here at the Ministry?  
**AI:** We are almost there in understanding that ‘digital first’ is part of the everyday approach to anyone working in the field of health, in addition to making regulations and where to put the money. Secondly, bringing the economic aspect to it was frightening at first, but now the management is very supportive and looks at opportunities to protect investments.
MORE DIGITAL; MORE COLLABORATIVE

Kristin Raudsepp, director general of Estonia’s drug regulator – the State Agency of Medicines – discusses her organization’s mandate, current priorities, and reactivity to the pervading trends in international regulation.

**HCLS:** What would you say are your main priorities right now?  
**KRISTIN RAUDESEPP (KR):** We hope that in the future the network of EU Medicines Agencies will strengthen and more IT solutions will be developed together, with the needs of smaller agencies considered as well. We are going to contribute to the regulatory optimization - less national requirements, optimised and simple processes and more work-sharing.

One of the main tasks for the next five years is the data standardization - ISO developed new standards for the identification of medicinal products (IDMP) which should be used worldwide. The five ISO IDMP standards should simplify the exchange of information between all stakeholders, enhancing interoperability of systems at the European Union (EU) level and internationally. Estonia represents small agencies at the EU Data Network Board which is taking part of the ISO/IDMP Task Force. For our agency, electronical data exchange is very important – we have to maintain everyday work with limited resources and our goal is to make our business processes as compact as possible and avoid any manual input of the data. The precondition for data exchange is standardised data and all the databases should speak the same language.

**HCLS:** Given that Estonia is a very small pharmaceutical market (EUR 240 million), what measures are you taking to incentivize innovation and incite international companies to bring their innovative products here?  
**KR:** It is very difficult to provide Estonian patients access to the very newest medicines given the pricing of these medicines is similar all over Europe. We do try to be flexible and work out solutions with companies that would satisfy both parties and would be affordable to Estonia. The promotion of generics is one instrument to free up assets for innovative medicines and careful deliberation on the cost-effectiveness of new medicines in order to ensure the most outcome for the Estonian patient is the other one.

**HCLS:** What would you like to tell your industry peers that will be reading this interview?  
**KR:** We are working hard to make the life of applicants easier, e-solutions are highly recommended and accepted in Estonia. The assessment fees are reasonable, including the assessment fee in MRP and DCP as Reference Member State. We use common EU systems where possible as it is not reasonable to create different systems/portals in all Member States. There are no country-specific requirements in Estonia for marketing authorization applications, these being harmonized with EU rules. We have a Client Portal for local users, for example Estonian representatives can send notifications about shortages and withdrawal of the MA via our portal.

Changes of rules are quick and smooth – in our small agency we have less bureaucracy, proposals and good ideas from our specialists and clients go live quickly. Estonia is an e-country, the agency offers more than 30 e-services. Our agency is involved in the development and maintenance of the national e-prescription system, which has been in operation since 2010. Today more than 90% of prescriptions in Estonia are digital prescriptions. ☺️
For many life sciences investors, the Estonian market exhibits many of the very same characteristics as its Baltic neighbours, but often played out on a miniature scale. According to mainstream forecasts, the pharma market is growing, but not necessarily to the extent that it would whet the appetite of many MNCs, especially when taking into account the volume limitations of a population numbering a mere 1.4 million.
BMI, for instance predicts total healthcare expenditure to increase from EUR 1.28 billion in 2016 to EUR 1.60 billion by 2020 while the value of the pharmaceuticals market is estimated to expand from EUR 310 million to EUR 409 million over the same time period equating to a CAGR of 5.7 percent in local currency terms. Yet Linas Dičpetris, EY’s advisory services leader for the Baltic States sounds a cautionary note. “Our advice when analyzing a minnow market like this is always to peer behind the statistics and dissect where that growth is coming from, because it may well be that the entire market is being driven up by the stellar performance of only a small handful of players,” he shrewdly ventures.

Juxtaposed against this positive growth trajectory, meanwhile, are familiar complications when it comes to securing market access for innovative medicine. “Unfortunately the reimbursement process is rather sluggish and it can commonly take up to five years to secure a final decision... while I am aware that this might compare favourably to Latvia and Lithuania, I personally feel that our ambitions as a nation should be higher and we should be striving to match countries whose net GDPs are similar to ours such as Portugal or Slovakia,” bemoans AstraZeneca’s market access director for the Baltics and country lead for Estonia, Kuuno Vaher.

The local health-financing context also reflects recognizable challenges relating to budgetary constraints. At EUR 1,407 per capita adjusted for differences in purchasing power, health spending in Estonia sits well below the EU average of EUR 2,797, while the percentage of overall expenditure on health as a share of GDP is also disproportionately low compared to European norms. “Just like in many markets across Europe, the population is aging and the epidemiology of the nation is shifting leading to an increase in patient need, which unfortunately is now beginning to outstrip supply. The disheartening reality is that Estonian healthcare accounts for a mere 6 percent of the GDP, which is fairly meager when you consider that a market like Slovenia is managing to sustain around 10 percent. At the end of the day, some countries value healthcare more than others,” contemplates Kadri Maegi-Lehtsi, the general manager of Roche.

Such a state of affairs often means the country has to scrap it out with its Baltic brethren competing head to head for finite investment inflows. “One major challenge for the local economy has been to attain a stabilization of foreign direct investment which, quite honestly, has not grown significantly in the past few years,” perceives Alo Ivask, chairman of the management board of Enterprise Estonia.

“While we successfully retained 12th spot in the World’s Bank’s ‘Ease of Doing Business’ ranking for a second consecutive year and consistently perform comparatively well on tax competitiveness indicators, there is a real risk of stagnation and flat-lining if we rest on our laurels,” he warns. “To my mind, keeping the same performance for a second year in a row must also be considered as a subtle signal of the need of improvement, and this news should really empower and urge us to strive to run faster,” he stresses.

That said, when it comes down to the basic fundamentals of market maturity, Estonia does clearly appear to be leading the pack within it’s own sub region. Estonian patients are spared, for example, the onerous co-payments and catastrophic out-of-pocket expenses so common in Latvia and Lithuania, with the state exchequer picking up the tag for more than three quarters of the public healthcare bill, and the autonomous Estonian Health Insurance Fund (EHIF)
renowned for its reliability and straightforwardness as core purchaser.

Moreover, under those circumstances when a patient is called upon to pay out of his or her own pocket, the willingness and ability to do so are normally there. “Your average Estonian is more affluent than his Latvian or Lithuanian counterpart, because purchasing power is greater and behaviorally he or she tends to attach a high value to wellness. As such, it’s not entirely uncommon to encounter patients coming forward and paying for their own knee replacement or hip operation,” remarks Sanofi country manager, Kai Hendrikson.

Maturity even seems to find expression in the policy making and political decision-making. “When I consider the differences between the Baltic States, the first specificity that springs to my mind is the stability of each marketplace. Estonia is by far the most stable in terms of the endurance of the political framework and the enlightened governance, whereas both Latvia and Lithuania have been experiencing a certain amount of turbulence from the enactment of sweeping reform processes and a revolving door of health ministers,” muses Roland Lepik, cluster head of the Baltics at Sandoz.

Indeed, what perhaps stands out and differentiates Estonia most of all is how a succession of e-savvy governments have been turning the country into a laboratory and testing ground for digitalized life sciences and connected health. “Our country is an outlier and trendsetter in the very pure sense of the words...We were the first nation to ever hold elections via the Internet, the first to offer “e-residency” for

The victim of a major cyber-attack in 2007, the first known on an entire country, that took down internet sites and servers of media outlets, banks and government bodies, Estonia has rebounded strongly by investing heavily in cyber security. To do so, the government of Estonia joined forces with Guardtime, a leader in cyber security using blockchain’s Keyless Signature Infrastructure (KSI), to provide authentication on a massive scale. The country has subsequently won great acclaim for being an early pioneer in the adoption of blockchain, notably enabling its citizens to use their ID cards to order medical prescriptions, vote, bank, apply for benefits, pay taxes and access approximately 3,000 other digital services. Even more interestingly, blockchain-like technologies have simultaneously been harnessed to secure health records and underpin the shared government database system, ‘X-Road.’

“The risk is not just cyber-attacks, but also people not being careful enough! In Estonia, private health data therefore do not sit in computers or mobile phones, but in secure servers. Patients do not have to carry the data with them either. The electronic ID is only a way to access those data,” assures Ain Aaviksoo from the Ministry of Social Affairs.

Meanwhile civil servants have been empowered to encrypt documents, review and approve permits, contracts and applications – security functions deemed necessary given that the Estonia today enjoys the distinction of being one of only a handful of digital societies to have digitalized one hundred percent of its citizens’ medical health records. “We are using blockchain as an additional layer of security to help us ensure the integrity of health records. Privacy and integrity of healthcare information are a top priority for the government and we are happy to work with innovative technologies like the blockchain to make sure our records are kept safe,” explains Artur Novek, implementation manager and architect of the Estonian E-Health Foundation.

Deploying a form of ‘permissioned blockchain’ technology (in which certain access is restricted in order to secure data and protect users’ privacy), time and resources expended verifying members’ trustworthiness have been vastly reduced. Such a feat may be difficult to scale up and emulate across the world however. “It can be much easier to construct a digital society if you are a small country, have no existing legacy systems in place and are able to start right from scratch,” cautions Kaspar Korjus, head of Estonia’s e-residency program.
Anyone in the world, and among the first to propose a national crypto-currency. While we are already appreciated internationally as a pioneering IT hub, many people in the life sciences domain are just beginning to grasp the exciting developments that we are putting into play around electronic health record keeping, bio-banking, medical genomics and personalized medicine through the smart application and use of digital technologies, enthuses Alo Ivask. “Come to Estonia and you will be thoroughly amazed!” he promises.

PIONEERING CONNECTED HEALTH

Estonia has indeed invested intensively in e-health and is now internationally recognized for its innovations. Most local health care providers keep an electronic health record for patients and all health care providers are responsible for sending patient health and health care service provision information to the central health information system. This allows patients to access their health data and providers to access and exchange information with various, relevant databases. Moreover, the system also allows for e-consultations, digital referrals and e-prescriptions with pharmacists increasingly tending to sell on-line.

“The Estonian e-health solution is quite unique in the world as it can be used not only by all healthcare professionals and patients, but its users also have the option of granting others access to their e-health data. Patients can give consent to allow the data in the health information system to be used in having a disability attested, to have their capacity for work assessed, or to assess their health before military service. These solutions save valuable time. When a person has gone to the doctor and the data exists digitally, the information can be reused. This helps avoid unnecessary tests and patients no longer have to present paper documents,” says Riho Tapfer, director of the Association of Pharmaceutical Manufacturers of Estonia (APME).

Aggregating and reusing health data can also be valuable in health sector management where it is important to analyze the effectiveness of treatments and other necessary indicators to organize treatment financing or ensure that healthcare is accessible. “There are a lot of data that the health insurance has at its disposal. In hospitals, for instance you can view every single bill and every single injection per indication. These data can be accessed and visualized by doctors. This is exactly what is needed in Estonia to render the system even stronger and efficient,” attests Kristin Raudsepp, director general of the State Agency of Medicines.

A multitude of fresh initiatives are also in the offing. Notable applications currently under development include an electronic immunization passport, a central digital registration system for outpatient care and, since 2016, a facility to provide access to claims and costs. The use of the platform has increased rapidly with 4.5 million enquiries from the patient portal to the e-health system in the first 4 months of 2017 compared to 0.5 million in 2011.

“This year we are opening up a health information system, which was built in 2007 for medical service providers to have access and share patients data between themselves. A start-up is piloting this project and is actively working on opening up the service and the data collected by the public healthcare system through mobile devices. This is possible because all Estonians have digital IDs and most of them use them via their mobile phone,” reveals Aaviksoo.

Another eyebrow raising development has been the formation of a dedicated ‘Connected Health Cluster’ as Estonia seeks to lead the way in re-conceptualizing healthcare provision by embracing the digital revolution and the internet of things and applying it to the clinical and care settings. The core idea is to get stakeholders interested in this space together so that cross-pollination of ideas can occur and so that digitally minded life sciences startups receive the support that they need so as to be able to commercialize their ideas.

“We are part of the Science Park Tehnopol and currently count about 70 organizations among our members. The cluster offers them incubator facilities, common space and everything else they might need in terms of business development. It goes beyond merely hooking up healthcare developers, because our members also
constitute universities and healthcare service providers, a few big hospitals and, at the policy level, we also have the Minister of Social Affairs as well as our health insurance fund,” explains Piret Hirv, health technology division manager at Tallinn Science Park Tehnopol and leader of the cluster. “Up until now, we are being financed by Enterprise Estonia together with membership fees and selling services and we see companies joining and leaving, depending on their needs. I do believe, however, that we are still lacking a big piece of the jigsaw: the consumers.

At the moment, we do not have active participation on behalf of citizens or patient associations, for instance, and that is something that we are obviously looking to rectify as quickly as possible,” she adds.

PEDDLING E-HEALTH INTERNATIONALLY

Interestingly Estonia’s ambitions to reshape healthcare using cutting edge digital technologies stretch far beyond national frontiers and seek to influence the uptake of e-health concepts abroad. One of Estonia’s priorities for the rotating presidency of the European Council was actually “the creation of a digital Europe by developing cross-border e-commerce and e-services for the benefit of consumers, producers and businesses.”

“During our presidency of the European Council, we proposed to the European Commission a political objective – the so-called ‘100 Million Connected Healthy Europeans’ initiative – for health and data relating to cooperation at the European level. This initiative is effectively a strategic moonshot goal for Europe, which is capable of stimulating

Integration and Trust: Vital Ingredients

Well functioning e-health is about much more than just possessing the right equipment, but additionally about properly mainstreaming processes and shifting the paradigm in how stakeholders go about interacting with one another. Naturally, change management and the deft winning over of hearts and minds are areas in which Estonia is excelling as manifested by the fact it only took 8 months to introduce and fully implement e-prescriptions.

“E-health, in the Estonian context, has become a great enabler and catalyst to breaking away from the status quo and doing things better. It facilitates access to a wide spectrum of interactive activities that extend well beyond just the optimum allocation of medicines,” reflects Ain Aaviksoo from the Ministry of Social Affairs.

“What we have created here today is not only robust infrastructure, but crucially a supportive legal framework and culture of belief and trust. Without these elements we simply wouldn’t be able to fashion the requisite levels of integration to allow e-health to work in practice. To become a genuine early-adopter of technology requires embedded commitment from a broad spectrum of stakeholders,” he affirms. By way of example, he refers to the cultivation of a highly supportive societal context in which some 80 percent of citizens have registered their approval of the biobank and gene mapping. “Estonian people really want this to happen. There is considerable trust in technology with almost everyone seeing the value in it,” enthuses Aaviksoo.
With its well-rounded infrastructure and reputation for scientific rigor, it is perhaps hardly surprising that Estonia, despite its diminutive size, should also present itself as a strong candidate as an affordable clinical trial destination country. “If we carry one real advantage compared to many other countries in the EU, then it is surely the attractive combination of real clinical excellence mixed with cheap operational costs,” reflects Riho Tapfer, director of the Association of Pharmaceutical Manufacturers of Estonia (APME).

“Globally, we find that the cost-quality ratio in Eastern Europe is one of the best in the world and Estonia is no exception when it comes to clinical trials,” agrees Rauno Oja, the managing director of the Estonian affiliate of EGreen. “The development of the healthcare system in our region is picking up and, in many instances, now equals that of Western European countries, yet the costs are not anything like as high as markets such as France or Germany. Five years ago, the industry was tremendously excited about going into India to conduct clinical trials, but when troubling news came out of countries like that – whether that be fraud, a lack of quality standards being adhered or manipulation of data – there has been a bit of a change of heart. I believe that, in many respects, Estonia can be regarded as a clinical trials hub of excellence with reliable data, but at low operational expenses,” observes Oja.

“We specialize in carrying out many rescue studies for projects that were stuck in terms of enrollment and in rounding out global studies that have been running for a number of years... We like to think of ourselves as a very efficient company, not only in terms of costs but also when it comes to planning ahead and having specific recruitment programs in place, and I think the Estonian contextual environment somewhat lends itself to that,” he muses.

“I believe Estonia’s strength resides in the capabilities of data management, protocol design and statistical writing and it goes without saying that EGreen is pushing towards implementing more of these aspects into our studies. Providing a quick turnaround for our clients remains challenging and the key consideration for many clients, but I am quite confident we will continue to manage this well as this has been our way of operating for a number of years,” concludes Oja.
Europeans by 2025. Starting from 35 million rare diseases patients, we already have a system that tracks their files whenever they are sent to specialty care centers, which are often in another country, as to continue with the treatment in their home country,” discloses Aaviksoo.

TRAILBLAZING PERSONAL MEDICINE

Just as interestingly, Estonia would appear to have installed itself right in the driving seat of the personalized medicine bandwagon courtesy of an ambitious national gene-mapping program under the purview of the Estonian Genome Center.

“I reckon that we differentiate ourselves not only as an earlier mover, but also through having world-beating, one-of-a-kind cornerstone institutions,” argues Enterprise Estonia’s Alo Ivask. “Take for instance the Estonian Genome Center of the University of Tartu, where 5 percent of the genomics of the national population is kept. The primary task has been to establish a large-scale population-based Biobank for the research and development in human genetics and genomics, collection of population-based genetic and health data, and implementation of the results from genetic studies for the promotion of public health... Meanwhile our small size, sophisticated technological infrastructure, and relatively homogenous populace render us an ideal place to put this ambitious idea to the test,” he surmises.

Certainly the Estonian Genome Center does stand out from the crowd. While there are currently more than 120 biobanks worldwide, the vast majority of them focus on genomic research rather than personalized medicine and few possess a means to integrate large amounts of data into personal health on a national scale.

“We working upon a system where, at the moment, 5 percent of the adult population have their genome sequenced and linked with all the health data. This will increase to 25 percent of the population this year and we are aiming to reach 50 percent in three to four years’ time. This is a great asset as we try to attract in international drug developers and convince them to conduct their development work in Estonia,” proclaims Aaviksoo. “Deeper understanding of genetics, in tandem with technological progress, will drive an ever more personalised approach to healthcare. This is essential in an ageing society where antiquated financial models are already stretched... I am absolutely positive that in a foreseeable future, every individual will have their genetic information known, at least to their doctor,” he predicts.

Auspiciously, many MNCs do seem to be on the same page. “Estonia is rightly acclaimed for its excellence in e-health and genomics, and if we can properly draw upon these two magnificent assets and leverage them in the right way, then we can be one of the pioneers of personalized medicine, which is clearly where healthcare and life sciences are next headed,” predicts Roche’s Kadri Maegi-Lehtsi. “I do not think that there are many countries either within the EU or the rest of the world, whose governments have yet put in place an established strategy for personalized healthcare. We have already made a big head start with our governmentally-funded genome bank which is soon to contain as many as 100,000 profiles and this will be difficult for anyone else to rapidly emulate, because of the sheer time it take to build up the data. This sets us up nicely to be a hub and focal point for other countries and international businesses aspiring to operate in this niche.”
Andres Männik, chief technology officer at Icosagen, discusses the importance of becoming a ‘strategic partner’ for their customers rather than a mere service provider, their ambition to increase their production and the role of quality service as a way to even more success.

**FROM TECHNOLOGY TO PRODUCTS**

Andres Männik, Icosagen

HCLS: Andres, can you give our international readers an overview of Icosagen and your background?

AM: I have a background as a molecular biologist and during my studies I specialized in the papilloma virus. Prior to joining Icosagen, I worked for a Finnish biotech company for 10 years where I focused my research on DNA vaccines. Icosagen was founded in 1999 and originally it was a diagnostic company, performing diagnostics of various infectious diseases. The company was split in 2006 and the diagnostic side of the business was sold to an international company. The money coming from that transaction was invested in what is now Icosagen. Currently, we are trying to shift from being a technology development company to a product development company able to produce our own products, even if up until now we have worked very much as a service provider for pharma companies, 95 percent of which are international customers.

HCLS: What are the competitive advantages that ultimately draw the interest of new customers and partners to Icosagen?

AM: I would say our production capacity is unparalleled. We translate our customers’ ideas into proteins, we are passionate about producing recombinant antibodies and challenging recombinant proteins in mammalian cells, as well as developing premium antibodies for research and in vitro diagnostics. In addition to this, we are also incrementing our GMP production. We also offer recombinant protein production for immunization functionality testing and development of monoclonal and polyclonal antibodies, including partial humanization and recombinant antibody production in mammalian cell culture. As we operate in a very niche area, we have very little to fear in the Estonian market.

HCLS: We hear from other interviewees that Estonia’s competitive advantaged in the R&D space is the possibility to partner with universities for drugs research programs. What is your take on this?

AM: I believe this is true. Estonia is a very small country with a thriving R&D landscape. Despite the size of our nation, there are many institutions conducting research and development activities in the healthcare and life sciences segment. The largest public research university is the University of Tartu, followed by the Tallinn University of Technology, the Estonian University of Life Sciences and Tallinn University. Other large research institutions that perform high-end research are the Estonian Biocentre, the Tartu Observatory, the Estonian Literary Museum, the National Institute of Chemical Physics and Biophysics. For instance, in order to develop the above-mentioned papilloma virus drugs project, we are partnering with the University of Tartu in the framework of the EAS R&D program with more than EUR 1.4 million.

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