

FLANDERS INVESTMENT & TRADE MARKET SURVEY



Life science and biotech industry in Lithuania



December 2016

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Executive summary

With a yearly growth of 22% over the past 5 years, Lithuania's biotech and life science sector shows potential to become an innovative R&D hub in the Baltic States. Today 16 academic institutions, 15 R&D centres (such as science parks and innovation valleys) and more than 370 manufacturers operate in the Lithuanian life science and biotech industry. The Lithuanian government also aims to encourage further innovative development in this sector and has a target to spend 1.9% of its GDP on R&D by 2020. Besides EU-funds of € 218 million for business enterprises' R&D projects in Lithuania, beneficial tax and R&D incentives for foreign investors are put into place, making Lithuania the 2nd best European country to invest in. World market leaders on the biotech and health sector such as **Teva Pharmaceutics** or **Thermo Fisher** are already present in the Lithuanian market and continue to invest in local and successful research companies.

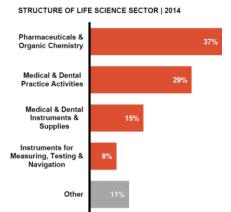
Yet local business investments in R&D account for only 0,24% of the GDP. Most Lithuanian enterprises do not expand to an international market, although some exceptions demonstrate profitable and international practices in biotechnology and laser industries. Lithuanian laser products account for more than 10% of the global market in laser technology, mainly due to its 40-year-history in laser physics research. Besides lasers, Lithuania's biotech research mainly specialized in pharmaceuticals, reagents and enzymes for molecular biology and recombinant pharmaceutical proteins (*red biotechnology*). Health technologies and biotechnologies are considered as priority areas for R&D support and led to success stories. For instance the advanced research concerning the Cas9/CRISPR genome editing technology that helps to identify and immunize bacteria and thus to edit genomes easily, means a major breakthrough in biology worldwide.

A few facts & figures

The history of the life sciences sector in Lithuania goes back to 1975 when the Institute of Applied Enzymology was established. The Institute quickly became a leader in the field of classical fermentation technology research. The name of the institute changed several times and in 1983 the focus of the institute's activities shifted to development and practical application of gene engineering methods. After Lithuania regained its independence, the institute was renamed into the Institute of Biotechnology in 1992. Due to its rich scientific heritage, Lithuania's biotechnology industry is outpacing developments in many larger Central and Eastern European countries.

Today Lithuania's biotechnology and pharmaceutical research and production sector knows an annual growth of 25%, with a 34% rate in yearly allocated funds for research and development (R&D) in the field. With **16 academic institutions, 15 R&D centres and more than 370 manufacturers** operating in the sector, science parks and innovation valleys, Lithuania already hosts one of the most innovative high tech hubs in Europe. Counting 3 million inhabitants, the country disposes of 23,300 specialists and researchers and 9000 students in the field of physics and life sciences. It is thus no surprise that Lithuania has one of the highest percentages of specialists with higher education among EU countries.

Over the past 5 years, sales in the **biotech and life science sector have grown by 22% each year**. **90% of manufactured products in the biotech industry,** that accounts for approximately 210 million euro a year **is exported** mainly to Germany, US, UK, France, Russia, Sweden and Japan.



The Lithuanian biotechnology sector developed mostly in the field of research in pharmaceuticals, reagents and enzymes for molecular biology and recombinant pharmaceutical proteins (*red biotechnology*). Experts in the biotech field developed for instance a method of cutting genes that is three times quicker and cheaper than any previously known technique. Yet Lithuania keeps also on investing in *green biotechnology*. **Biocentras**, a spin-off of the Institute of Biotechnology became a regional leader in the field and was nominated as a top five finalist for "Most Innovative European Biotech SME Award 2011".

Moreover Lithuanian laser products account for more than 10% of the global market in laser technology, as the country has a 40-year-history in laser physics research.

This established R&D base and the business climate supported by the Lithuanian government with tax incentives for investments into R&D encourage foreign biotech and life science companies to invest in the Lithuanian industry. The government aims the target of spending 1.9% of its GDP on R&D by 2020. Yet market-oriented research happens only to a limited extent, as investments of local only accounted for 0,24% of GDP in 2014. Moreover funding levels are not competitive with other European states, and most Lithuanian enterprises lack of international expansion, although some exceptions demonstrate profitable and international practices in biotechnology and laser industries.

Global key players such as **Thermo Fisher Scientific Inc.**, the absolute leader in serving science, and the Israeli company **TEVA Pharmaceutical Industries**, the second largest generic pharmaceutical company worldwide established research and manufacturing centres in Lithuania.

The following section of this market study gives an overview of the investment incentives that the Lithuanian government and the EU institutions provide for R&D and innovation in the biotech and life science industry.

State Policy to foster R&D and innovations in Life Science

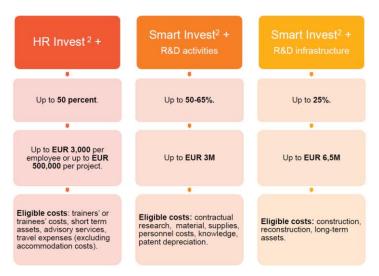
Fostered by EU funding, the Lithuanian government offers beneficial tax and R&D incentives for foreign investors and is recognized as the 2nd best country to invest in Europe.

More than € 600 million has been allocated from the EU Structural Funds 2007-2013 for Lithuania to develop Lithuania's R&D sector — namely, preparation of specialists of the highest qualification, modernization of the R&D infrastructure, as well as creation of favourable conditions for the cooperation between business enterprises and scientific institutions while promoting cutting-edge technology transfer and implementation of innovations. A total of €

	LT	LV	PL	DE	SE
Corporate profit tax	0 - 15%	15%	19%	< 33%	22%
VAT	21%	21%	23%	19%	25%
Dividends	0-15%	0%	0-19%	0-25%	0-30%
Personal income tax	15%	23%	< 32%	< 45%	< 57%
Social security tax	9% employee 30.98% employer	10.5% employee 23.59% employer	Total 35%	Total ~40%	7% employee < 31.42% employer

218 million from the EU Structural Funds' support has been assigned for business enterprises' R&D projects in Lithuania (investment into development of new products).

Health technologies and biotechnologies are considered as priority areas for R&D support, especially molecular technologies for medicine and bio pharmacy, intelligent applied technologies for personal and public health, and advanced medical engineering for early diagnostics and treatment.



This chart provides an overview of R&D incentives for foreign investors interested in locating R&D business in Lithuania as well as foreign companies already operating on the Lithuanian biotech and life science market but eager to further expand.

Requirements for R&D support depend mainly on the size of the investing company, its income, the project duration and the activity, as mentioned below.

Requirements for the applicant

- Investor's (including income of the investor's group of undertakings) annual average income for the last 3 years is ≥1 m €
- Investor invests into R&D ≥ 1 % of annual income
- Investor is involved in R&D activities for ≥ 1 years
- Applicant's project corresponds to the Lithuanian Innovation Development Programme for 2014-2020, i.e. the product/s created during or after the implementation of the project shall be new on corporate or market level, or on the global level, as specified in the Oslo Manual.
- Applicant's project activity falls within one of the Smart specialization programme sponsored activity sub-groupings (see Appendix 1)

Requirements for the project

- Project duration:
 - o Activity 1 up to 24 months
 - o Activity 2 up to 36 months
 - o Activity 3 up to 24 monhts
- Project value shall not exceed 50 m €
- At least 20% of new FTE positions will be dedicated for researchers. Created jobs shall be maintained for 5 years following the project implementation
- Project activities must be implemented in Lithuania

Eligible costs

- Expenses related to R&D activities (Activity 1):
 - Knowledge and patents bought or licensed from outside sources;
 - Costs of contractual research;
 - Costs of materials, supplies and similar products, incurred directly as a result of the project;
 - Depreciation costs of long term assets;
 - Personnel costs (including costs for business trips);
 - Additional overheads.
- Expenses related to R&D infrastructure (Activity 2):
 - Costs of construction or reconstruction;
 - Long term assets (furniture, computers, software, patents, licenses, equipment)
- Expenses related to process and organizational Innovation (Activity 3)
 - Knowledge and patents bought or licensed from outside sources
 - Costs of contractual research;
 - Costs of materials, supplies and similar products, incurred directly as a result of the project;
 - result of the project;
 Depreciation costs of long term assets;
 - Personnel costs (including costs for business trips);
 - Additional overheads.

Supported activites

- Activity 1: Applied research and development activities (Industrial Research & Experimental Development)
- Activity 2: A company's initial investment for building or expanding an existing enterprise R&D infrastructure
- Activity 3: Activities related to process and organizational innovations

NOTE: Aid Intensity shall not exceed 80 %

Activity 1: Aid Limits for Activity 1: 0,05 - 3 m EUR

	Support Intensity				
Activity 1	Large Company	Medium Company	Small Company	Effective Collaboration*	
- Industrial Research	up to 50 %	up to 60 %	up to 70 %	1 up to 150/	
- Experimental development	up to 25 %	up to 35 %	up to 45 %	+ up to 15%	

^{*} According to Commission Regulation (EU) No 651/2014, aid intensities for industrial research and experimental development may be increased by 15 percentage points if one of the following conditions is fulfilled:

Aid Limits for Activity 2: 0.05 - 6.5 m EUR

	Support Intensity			
Activity 2	Large Company	ge Company Medium Company Small		
R&D Infrastructure	up to 25%	up to 35%	up to 45%	

Aid Limits for Activity 3: 0.05 - 0.5 m EUR

	Size of a Company		
Activity 3	Large Company	Medium Company	Small Company
Process and Organisational Innovation	up to 15 %	up to 50 %	

How to determine the size of an Applicant Company

Company category	Employees	Turnover	or	Balance sheet total
Medium-sized	< 250	≤ € 40 m	≤	≨ € 27 m
Small	< 50	≤ € 7 m	5	≨ € 5 m
Micro	< 10	≤ € 2 m	5	≨ € 1,5 m

Please note, that the size of a company is evaluated by the level of the Company's Global Ultimate Owner (i.e. whole group size). The number of employees is equal to the number of positions (if one position is occupied by two half-time workers, they must be counted as 1 employee).

R&D valleys and institutions for Life Science

To integrate higher education institutions, research centres and businesses areas that work within specific scientific or technological areas, Lithuanian authorities have invested EU structural funds in 5 Valleys. These Valleys are Integrated Science, Studies and Business Centres (Valleys) in the country's 3 largest cities, Vilnius, Kaunas and Klaipėda. The valleys should provide a favourable environment for the transfer of scientific know-how and technology to the business sector.

The 5 Valleys are:

• Santara and Sauletekis Valleys (Vilnius) – biotechnologies, innovative medicine, biopharmacy, ecosystems, ICT, laser and light technologies, nanotechnologies, semiconductors technologies and electronics, civil engineering.

- Nemunas and Santaka Valleys (Kaunas) agro biotechnologies, bioenergy and forestry, food technologies, safety and wellness, sustainable chemistry and pharmacy, mechatronics, future energy and ICT
- Maritime Valley (Klaipėda) maritime technologies and maritime environment.



However, using this new research infrastructure efficiently remains a major challenge, and cooperation between industry and research organizations remains rather weak. The government has also supported the sector through financial incentives (in particular, an R&D tax credit for enterprises) and regulatory measures. Demand-side measures encouraging innovation are less developed. Excessively bureaucratic procedures are cited by the science and business communities as among the main obstacles to research and innovation in Lithuania. The government recently developed a new smart specialization strategy intended to focus resources on science and technology areas in which Lithuania can be internationally competitive, although it has been criticized for investing too heavily in the construction of new buildings and renovation of low-ranking university campuses.

Out of the 15 institutions, 5 institutes and 6 university departments conduct research in the medical biotechnological field. These 11 institutions are all reviewed below. Six institutions, including five major universities, train biotechnology and business specialists in cooperation with both domestic and foreign biotechnology companies. It is important to note that research with embryonic stem cells is not authorized in Lithuania. On the other hand, research with induced pluripotent stem cells (iPS) and adult stem cells can be performed.

The biggest scientific research centre in Lithuania is the **Institute of Biotechnology**, which was founded in 1975 and was renamed in 1992. The **Institute of Biotechnology** receives all its income from participating in international programs (the net income in 2008 was € 3,65 million). The institute has established a DNA sequencing centre in 2003 and performs research in: recombinant proteins, enzyme research, drug design, bioinformatics, immunodiagnostics, epigenetics and molecular diagnostics. The institute has 100 employees, out of which over half are researchers and scientists.

The Institute of Biotechnology (IBT) at Vilnius University collaborated in a multi-year research to advance the technical and commercial utility of guided Cas9/CRISPR genome editing technology.

This Cas9 technology will help to identify and immunize bacteria and thus to edit genomes easily. This major breakthrough in biology will promote drought tolerance and disease resistance consequentially protecting plant health and increasing crop yields.

The Institute of Biochemistry performs cell biology, biosensors and enzyme research: in 2008 the institute established a Proteomics centre. The Institute of Immunology has special facilities for research with experimental animals and "knock-out" mice. The institute also performs research on bio models and antibodies. The Institute of Oncology performs research on cancer cells and makes molecular markers of cancer cells. In 2009 the institute founded a biobank of tumor tissues. The Institute of Clinical and Experimental Medicine performs research on stem cells, regenerative medicine and autoimmune diseases. Recently, both institutes have been merged to form the Institute of Innovative Medicine. The institute is considered to be the best in stem cell research in Lithuania and is currently piloting a project with an institute in the USA. Vilnius University Department of biochemistry and biophysics, which was founded in 1962, is the second biggest research centre in Lithuania. The department closely collaborates with Western institutions and performs research on the photosensitization of mammalian cells and microbial resistance to antibiotics. Vilnius University Hospital Santariskiu Klinikos is the leading facility for clinical trials with patients. Kaunas University of Medicine conducts research on pharmacogenetics (personalized medicine), epigenetics, polymorphism of genes related to cancer, cardiovascular diseases and regenerative medicine (for cardiac diseases). Kaunas University of medicine is investigating the possibility of using stem cells to help revive a heart that has been damaged by a heart attack. The first stem cells have already been tested on a famous rabbit named "Roger". Vilnius University Department of Medicine researches gene polymorphism in Lithuanian population and atherosclerosis risk factors. Vilnius University Department of Chemistry specializes in nanotechnologies and new analytical systems. Vilnius Gediminas Technical University Department of Biochemistry and Bioengineering models biocatalytic systems and performs researches the immobilization and refolding of recombinant biopharmaceutical proteins.

The Lithuanian Biotechnology Association (LBTA), established in 2003, is one of the main promoters of the Industrial Biotechnology Program in Lithuania for 2007-2010. The association has more than 60 members, including 56 physical members and 7 legal entities. It also has representatives in ESAB (The European Federation of Biotechnology) and is attempting to join the EuropaBio. The Lithuanian Biotechnology Association is also the main promoter of the Lithuanian National Biotechnology Platform.

Major players in the Lithuanian biotech and life science market

TEVA Baltics/ Sicor Biotech UAB - www.eng.tevabaltics.com

TEVA Baltics/ Sicor Biotech UAB became a part of TEVA Pharmaceutical Industries in 2006, when TEVA acquired the American biotech pharmaceutical company Sicor Inc. As Sicor Biotech is originally a Lithuanian company, it represents TEVA, 2nd largest pharmaceutical company worldwide, in the Baltic region.



While TEVA focuses on the production of specialty, generic and over-the-counter (OTC) medicines, Sicor Biotech develops mainly recombinant biopharmaceuticals using advanced research and production technologies and conducts research in biochemistry, molecular biology, modern genetic engineering, biosynthesis and development of biopharmaceutical products. Sicor Biotech has built a global reputation for its **medicine treating cancer diseases** such as Filgrastim, Tevagrastim and Radiograstim. The company is also known for its revolutionary method of **cutting genes by using enzymes** 3 times faster and cheaper than the best previously known methods. Other activities of Sicor Biotech are the **production of insecticides and repellents, and medical devices**.

As Sicor Biotech is investing € 36 million in the expansion of research and production capacities, the installation of new quality control and R&D laboratories, and new manufacturing lines, the company has already invested more than € 1,2 million in a new research centre to combine research and production in one facility. Exports of Sicor Biotech, the largest biotech company in Lithuania, grew by 68% in 2014. Sicor Biotech exported more than 98% of its manufactured products and was named Lithuanian Exporter of the Year by the Lithuanian Confederation of Industrialists. Currently, Sicor Biotech supplies products to more than 50 countries worldwide, mostly to the United States of America, countries of the European Union and Japan.

Thermo Fisher Scientific Baltics UAB - www.thermofisher.lt

World leader in serving science, Thermo Fisher Scientific. Acquired Fermentas, a Lithuanian manufacturer of molecular and cellular biology products for € 242 million, in 2010.



In 2011-2012 Thermo Fisher Scientific invested € 13 million to build an additional 10,000 m² for R&D, manufacturing, warehousing and other functions to further enhance the capabilities of the **Vilnius Center of Excellence for Molecular Biology**. The site enables the company to showcase its capabilities for developing and manufacturing products used in a range of life science applications, providing molecular, protein and cellular biology products to meet customers' growing demand in Eastern Europe. Thermo Fisher has hired this year **110 additional specialists** to expand its manufacturing department in Lithuania. Among the 710 employees, 90 researchers work in R&D centres.

Fermentas Molecular Biology Solutions include restriction enzymes, nucleic acid purification kits, reagents for PCR, quantitative PCR (qPCR) and Reverse Transcription as well as a wide variety of other molecular biology enzymes and reagents.

Viltechmeda/Aitecs - www.moog.com

In 2009, **Moog Medical Devices** acquired the Lithuanian company called Viltechmeda. The American Moog group invested in 2010 in an additional service centre to expand its research and technology brand in Lithuania. Since 1993, Viltechmeda manufactures, sells and repairs medical equipment, devices for infusion and syringe pumps. Those



advanced medical technologies are used in anaesthesia, neonatology, oncology, surgery, intensive care and other medical areas that require very precise dosages of medicines. Viltechmeda or AITECS Medical UAB remains one of the **leading producers of high tech medical devices in Europe** with 90 employees in Lithuania.

Biotechpharma - www.biotechpharma.lt

Biotechpharma was established in 2004 and is the only contract development and GMP-compliant manufacturing organization for biopharmaceuticals in the Baltic states. The company



focuses mainly on recombinant protein technology development. In 2011-2012 the company invested in an additional state-of-the-art R&D laboratory and a biopharmaceuticals manufacturing centre. Biotechpharma employs now 120 people in Lithuania and generated in 2015 a turnover of approximately € 15 million, with a 100% of export shares.

Other players in the Lithuanian life science and biotech market

Valeant - www.valeant.com

Valeant Pharmaceuticals International is a Canadian pharmaceutical company that specializes in neurology, dermatology and



infectious illnesses treatment for preparations. In 2013, the company acquired a pharmaceutical factory **AB Sanitas**, that actually offers more than 50 different products. The Lithuanian team consists of 115 high-skilled specialists, which makes Valeant in Lithuania one of the fastest growing pharmaceutical producers in the region.

Intersurgical - <u>www.intersurgical.lt</u>

Intersurgical is a leader in Europe in providing respiratory care equipment and tools. The company was founded in 1982 in the UK and during its



expansion, Intersurgical opened a unit in Pabradė in 1994, Lithuania. The company produces and supplies 4 products for oxygen and aerosol therapy, anaesthesia, resuscitation and the respiratory system. These products are mainly used in hospitals, operating rooms, intensive care units, and other postoperative hospital wards, ambulance and at home in more than 100 countries. In 2016 Intersurgical is one of the largest employers in Pabradė with a team of more than 1,900 employees.

Biocentras UAB - www.biocentras.lt

JSC 'Biocentras', a spin-off of the Institute of Biotechnology became a regional leader in the field of green biotechnology. The scientific-industrial company generated in 2015 a turnover of approximately € 1,5 mio.



Profarma - www.profarma.lt

Profarma was founded in 2007 by leading biochemistry scientists from TEVA Pharmaceuticals who led the development of Tevagrastim and is one of the first biosimilars in the EU. The company has a portfolio of 7 cost-efficient biosimilar technologies offered for out-licensing, has 2 technologies already



out-licensed and a pipeline of 4 biobetter technologies developed using patented ProMER™ platform, that allows extending biopharmaceuticals' circulation half-life in plasma.

Profarma mainly focuses on wave 3 products (with patents running-out after 2020), disposes of **EU cGMP certification** for batch release and analytical testing and has access to **cGMP manufacturing** to supply clinical and commercial needs.

Vittamed - www.vittamed.com

Vittamed is a neurodiagnostic medical device company with offices in Kaunas (Lithuania) and Boston (USA). The company has developed the world's first accurate non-invasive absolute intracranial pressure meter. Vittamed also created a suite of ultrasound-based devices to non-invasively measure real-time cerebral blood flow autoregulation



(CA) and **intracranial volumetric wave monitoring**. The non-invasive diagnostic methods have been clinically tested and proven in leading neuro centres in Europe and the United States.

Current methods for measuring intracranial pressure (ICP) are invasive and require drilling a hole in the skull to insert a sensor (TBI patients) or a lumbar puncture (neurological patients). These procedures are both risky and very expensive. Vittamed's non-invasive technology provides a safer, more cost effective way to capture the same clinical information for doctors and is less traumatic for patients.

NASA is currently exploring whether Vitttamed's device may help how to assess non-invasively and reliably intracranial pressure as some astronauts are developing serious visual impairment conditions with associated symptoms suggestive of elevated pressure on the brain.

Bioseka UAB - www.bioseka.eu

This biotechnology company started in 2011 developing antimicrobial oligonucleotide biotechnology and measuring of antibiotic-resistant bacterial infections control.



In 2015 Bioseka, scientists from Vilnius University School of

Medicine and the Israeli biotechnological business "GeneArrest" gathered together to create a new antibacterial biotechnology for the treatment of life-threatening infections.

Life Science and biotech events in Lithuania

Life Sciences Baltics - www.lsb2016.com is the only international forum in the Baltics for world-class biotechnology, pharmaceutical, and medical devices experts from all around the world. It provides an opportunity to explore the new horizons partnerships, exchange ideas and seek progress through networking. This event takes place in Vilnius each



Life Sciences Business Lab is a cycle of monthly meetings for entrepreneurs and scientists, interested in life sciences, to share news and trends, connect science and business or even establish new life sciences startups. The main goal of these events is to foster the Life Sciences Start-ups ecosystem in Lithuania.

Conclusion

second year.

Despite the lack of effective and profitable cooperation between R&D institutions and companies, the life science and biotech sector in Lithuania can ascribe major R&D accomplishments such as the development of enzyme cutting genes Filgrastim and Tevagrastim, the advanced research concerning the Cas9/CRISPR genome and the developed laser industry. Lithuanian laser products account today for more than 10% of the global market in laser technology.

The Lithuanian state policy, mainly supported by the EU, creates a business climate with tax, R&D and investment incentives which makes Lithuania the 2nd best European country for foreign capital to invest in. World market leaders in the biotech and health sector such as Teva Pharmaceutics or Thermo Fisher and smaller research companies, for instance Valeant and Intersurgical, are already present in the Lithuanian market and continue to invest on local and successful research companies.

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Date of publication: December/2016