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Picture courtesy of Jürg Züürcher ©
Mouth of the Trollfjord, Norway
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This year’s report discusses the increasing levels of complexity in the field of biotechnology. And it explains how this is driving exciting change in the Swiss biotechnology sector. The take ranges from the insights of an evolutionary biologist to news of the latest programs and institutions.

Switzerland’s success in biotechnology relies on the diversity of its knowledge networks in research, industry, finance and industry development. They are vital because the advances in science and technology is making the study of complex living organism exponentially more complex.

To live with and benefit from this complexity is the great challenge and opportunity moving forward. So it is essential for a successful biotechnology ecosystem to find the right answers, to develop promising strategies and to have insight and clarity of vision. The Swiss biotechnology sector has the best requirements to transform this complexity, as an enabler for innovation and digitisation, into economic growth – also, because Switzerland is working hard to stay an ideal base for biotechnology businesses.

Johann N. Schneider-Ammann
Federal Councillor of the Swiss Confederation
Living complexity and the role of trusted networks

Life sciences deal with living organisms, which are complex self-organizing systems. This complexity increases exponentially when we take life sciences out of the laboratory and incorporate them into the world of living beings. Living beings are organized into communities that make up societies and the economies that govern the way that people and organizations trade and interact. And this applies at a local, regional, national and global level. Each new dimension provides another layer of complexity.

Complexity as such need not be a problem. On the contrary, the more complex the system, the greater the capacity for knowledge and insight. Thanks to open access and open data, scientific findings are more available than ever on a global scale. This applies to natural sciences, engineering and technology, medical and health sciences, agricultural sciences, social sciences and humanities.

Information and communication technologies provide the means to democratize knowledge by spreading and sharing information in real-time. And this is vital! Staying up to date with new developments and having access to relevant content and information is crucial in maintaining and developing a nation’s capacity for innovation.

This is why the OECD scoreboard recognizes ‘Empowering Society with Science and Technology’ as an innovation driver with criteria such as connectivity, online devices, user sophistication and much more. These criteria complement the more traditional indicators such as R&D spend, quantity and quality of research staff, patents and publications.

However, the very technology that makes managing and sharing complexity possible, is also a potential conduit for dirty data and fake or hoax news. In this new age of fluid communications and big data, what can we trust and how do we ensure that we are not being misinformed? Could it be that the constantly increasing volume of data is not a measure of innovation and knowledge creation but rather the fuel that powers complexity at the expense of insight? The reality is that today we are exposed to more information than we can healthily digest.

To counter this, we turn to strategies that help to reduce and manage complexity. We simplify, fragment and compute data, not just in our professional lives, but also in our private lives. Increasingly we rely on search and filter algorithms to orientate ourselves within the avalanche of new data. Filter systems and search machines are becoming the central interface between science, society and economy; sometimes replacing institutional directories with open source solutions such as Google Patents. Individual and traditional experience is just not up to managing today’s complex situations.

Moving forward, continuous learning and the role of intuition and instinct may continue to be part of the solution but as it becomes more difficult to find reliable and quality proven information, the importance of knowledge based services and research areas will increase.

The reason why we need sustainable and reliable ‘knowledge networks’ is clear. Only through these can we hope to cope with key developments and the vast amount of data associated with them; the increase of our scientific understanding of systems; the integration of global societies and cultural diversity; the development of the internet of things. Good knowledge can foster and enable exchange between disciplines and sectors and work at the interfaces; collecting and condensing information to support innovation.

In this year’s report we have an article by the Swiss National Science Foundation, wherein scientist and author Andreas Wagner argues that complexity in living organisms usually allows for greater innovation and also creates an internal robustness to change; it tends to generate a range of alternatives like ‘multiple routes to one destination’. Counterbalancing this view, we have an article by Six Swiss Exchange that calls for greater clarity to make sense of complexity within man-made organizations: “Companies that master a structured approach to reduce complexity will unlock new opportunities ... not only will they, become more effective, they will also be better understood.”

The Swiss Biotech Report 2017 brings together knowledge networks in research, industry, finance and industry development to provide essential insights into the way in which the sector is evolving. The key issue is not so much managing complexity but living it! By identifying and using relevant data we can further science and technology toward innovation and on the back of this deliver relevant solutions for society.

We hope you find this a faithful report on the year past and a useful guide to the year ahead.
Andreas Wagner, Professor for Evolution at the University of Zurich and the Santa Fe Institute in New Mexico

Interviewed by:
Florian Fisch, Science Editor Swiss National Research Foundation

“Complexity allows for innovation”

Evolutionary biologist Andreas Wagner knows it from his own research: life is hard to understand because of its complexity. But without the intricacies of metabolisms and intertwined protein structures, organisms would not have enough freedom to innovate.

Many people seem to be overwhelmed by the current speed of technological change. But is the world really getting more complex?

If you ask my opinion as a citizen, the answer is clearly yes. There are many indications: the number of websites increases, as does the interconnectedness of mobile devices and communication networks. However as a biologist, I cannot really give you a definite answer.

You mean as to whether organisms are getting more complicated through evolution?

Yes. There is a longstanding debate among evolutionary scientists as to whether the complexity of life has increased throughout history. Common sense tells us that yes, an elephant is more complex than an Escherichia coli (E. coli). The bacteria’s metabolism is in some ways simpler than ours. We are able to make products that E. coli cannot – take steroids for example. But then we are unable to produce the eight vitamins that E. coli makes for itself. So we cannot tell for sure where metabolic evolution goes.

How can you measure complexity in biology?

There is no accepted way of measuring it, as there is for example in computer science. There you have clear and universal features of computational complexity: the number of operations per time or stored data elements. In biology you can count the number of cells. So a roundworm would be more complex than a bacterium. But some argue that it is rather the number of cell types that counts. Then again, the organization of cells seems to be more important than their bare number.

Which measure do you favour?

I would definitely not push for a universal definition. Some quantities are useful operationally for specific questions or systems. For a metabolism, which is really a network of chemical reactions, more reactions certainly entail more complexity. But then this neglects the fact that some enzymes are highly regulated. Simply counting them would neglect this level of complication. We are currently working on new definitions that are especially useful to understand how evolution innovates.

Which are?

This is not published yet, so I prefer not to talk about it.

Would you say that complexity is a defining feature of life?

(Hesitates) If you take complexity as the union of many different parts, then yes.

You say that innovation depends on complexity. How?

I was hoping for this question. Usually every engineer tries to avoid complications as much as he or she can. The reason is clear: a simple electronic circuit or mechanical device is much easier to produce, more efficient in maintenance, breaks down less frequently and is more accessible to understanding. But our research showed that complexity in living organisms usually allows for innovation. This is because it creates an internal robustness to change; for example when a mutation occurs in a gene or the environment of the organism changes. In this sense E. coli is very robust as it can live on dozens of different carbon sources...

...like a backup plan?

It is not so much about backup, but about alternatives. I like to compare it to the motorway system in a big city. A backup is comparable to multiple lanes on one road. But there are also multiple motorways going to many different places. When one breaks down you can find a route via other roads. I call it distributive robustness.

And where does innovation come into the equation?

This internal flexibility allows new things to arrive. It becomes easier to change one part without shutting down the whole thing or bringing it to a collapse. This ability to tinker makes robustness important for innovation. For example, we studied and classified them according to the robustness of their struc-
tured to mutations. Then we checked how many different activities each type of structure had evolved and used this number as a measure of past innovation. It became clear that robust enzymes had experienced more innovation. Nonetheless, I must say that we do not have a direct link between complexity and innovation in enzymes.

“With robustness it is easier to change one part without bringing the whole thing to a collapse.”

Are complexity and innovation more clearly linked in metabolism?
Yes. We know of bacteria related to E. coli that lived inside the cells of aphids for 50 million years. They have a very simple metabolism and their development has been evolutionarily stagnant and they have not been doing anything interesting for a long time. In contrast, even different strains of E. coli have very divergent metabolisms.

For understanding things you have to simplify. How do you go about studying nature’s intricacies in your research?
I use the same strategy that scientists have used since the enlightenment. First, identify the simplest possible incidence of your research problem or create a mathematically very simple model. We call it a toy model. Then, start by getting a feeling for it to inform your intuition. Starting from this intuition, you can begin to understand more complicated cases.

You wrote books for the lay public. Did you ever fear oversimplification?
I guess every scientist who is writing for the general public knows that feeling. In every simple sentence I agonise whether to add more nuance and risk losing the reader, or add less and have a problem with my conscience. In my last book, I added lots of end notes to circumvent the problem, but you cannot do everybody full justice.

Let’s talk about big data. Is it more of a blessing or a curse?
Take genomics as an example. Some scientists are frustrated by the limited knowledge that sequencing the human genome provided for medical science. But imagine the pre-2000 world without the genomic data: whenever you worked with a gene you had to find and sequence it and you did not know whether there were similar ones in the genome. This problem is now gone. So big data is absolutely a blessing. However, to make full use of it we have to shift focus from data generation to creating ways of analysing the data. And indeed, universities now hire an increasing number of professors for data analysis who are able to integrate theory and experimental data.

What recommendation would you give to biotech entrepreneurs?
Complexity is good and can be harnessed. The price that it is harder to understand is well worth paying. People should think about designing complexity into their systems so that they are more robust and ready for innovation. A practical example is robust proteins that can function in different cellular environments. In life’s evolution such proteins have brought forward more diverse abilities than their more delicate counterparts. They can also evolve new functions better in the laboratory. This is an example of how basic research can have real life implications.

Dedicated to understanding evolution
Andreas Wagner is Professor for Evolution at the University of Zurich and the Santa Fe Institute in New Mexico, dubbed ‘the world headquarters for complexity science’. Born in Austria he was a biology graduate student in the USA and received his PhD from Yale University. After 16 years on the other side of the Atlantic, Andreas Wagner now lives in Zurich with his wife and son. He is a member of the Swiss Institute of Bioinformatics and leads a laboratory of 18 people dedicated to both the computational and experimental approach to evolution. He has received various prizes and has written two popular science books; the most recent being The Arrival of the Fittest. Andreas Wagner’s research has been funded by the Swiss National Science Foundation (SNSF) on many occasions. For further information on SNSF funded projects visit p3.snf.ch

Funding excellent research
The Swiss National Science Foundation (SNSF) is the most important Swiss agency promoting scientific research. As mandated by the Swiss Federal Government, the SNSF supports basic research in all scientific disciplines, from philosophy and biology to the nanosciences and medicine. The focus is on the scientific assessment of projects submitted by researchers. The best applicants are funded by the SNSF to the tune of around CHF 880 million each year. The SNSF supports close to 3,400 projects involving 14,800 researchers annually. For further information visit www.snsf.ch
Industry and research harvest the fruits of the NTN Swiss Biotech program

The NTN Swiss Biotech™ is a unique network that supports the competitiveness of the biotech ecosystem, fueled by close ties between industry and research and sponsored by the Commission of Technology and Innovation (CTI).

The NTN (National Thematic Network) Swiss Biotech™ has set some ambitious objectives which are important when it comes to adding value to the technology value chain:

- combining core competences of absorptive companies with academic knowledge and practices;
- bringing together decentralised competences such as academic partners and industry;
- concentrating knowledge and technology around platforms;
- supporting the building up of important alliances;
- enabling access to a reliable network of capacities.

The NTN Swiss Biotech™ makes use of effective instruments to implement the set objectives:

- organizes events to bring industry and research together such as the Swiss Biotech™ Day (including partnering), the Swiss Biotech™ Innovation Day, the Swiss Biotech™ Research Day at Basel Life, the Swiss Biotech™ Day Fall and specific platform events;
- provides platforms to concentrate knowledge and technology from antibiotics to tissue engineering;
- brings together decentralised competences and chaperones the phase of partner finding;
- supports international activities and participates with an exhibition stand at events such as BioEurope or BIO Convention;
- promotes events, workshops, successful R&D projects through own publications (NTN bulletins), articles in journals such as European Biotechnology or CHIMIA and website coverage (www.biotechnet.ch, www.swissbiotech.org);
- provides seed money to realize CTI projects.

Since it was established in 2013 the NTN Swiss Biotech™ has stimulated exchange and interaction between industry and academia. These are a selection of successful R&D projects:

**High added-value diagnostics**

BOHLMANN Labs is a sound source of innovation. Within the CTI Special Measures for the strong Swiss franc, the team, together with two Swiss companies and the FHNW, created CALEX®, a stool extraction device that enables stool extracts to be prepared for biomarker tests outside medical laboratories; for example in POC settings or for self-testing (two patents pending). The MIAMI project in the 7th Framework Program with Swiss and European partners generated IBDoc®, the first IVD CE marked self-test to help with the therapeutic monitoring of diagnosed IBD (inflammatory bowel disease) patients.

**Member competences in NTN Swiss Biotech™**

At HES-SO Valais-Wallis, Prof. Fabian Fischer has specialized in microbial fuel cells for novel applications that meet the challenge of producing renewable energies. He and his team possess a unique expertise in bioelectric energy vector generation, phosphate extraction and the testing of antimicrobial surfaces.

Peptides are small proteins typically containing a chain of up to 100 amino acids. In our bodies, they are produced every day in vast quantities and perform highly specific biological activities. As there is an increased interest in peptides for pharmaceutical applications, the HES-SO Valais-Wallis created a research group to focus on peptide and protein technologies.

For the first time, researchers from MCI Innsbruck and the University of Salzburg have manufactured and purified a plant-based allergen in a green algae and opened the door to a specific immunotherapy against allergies. Their vision is to replace unpleasant injections with oral administration, as its production is both simple and cost effective.

In summer 2016, Michael Raghunath from the National University of Singapore (NUS) took over the professorship from Ursula Graf-Hausner in cell culture technology and tissue engineering at Zurich University of Applied Sciences (ZHAW), Life Sciences and Facility Management. He intends to boost 3D tissue engi-
neering with his core technology of macromolecular crowding and spur on the development of bioink for bioprinting. He will introduce metabolic tissue engineering as a research theme in Switzerland with the aim of making an impact at national and international level.

Networking events by NTN Swiss Biotech™
The NTN Swiss Biotech™ Innovation Day demonstrates the potential of industry-academia collaborations for innovation in life sciences. Program highlights were the keynote by Dr. Peter Grunenfelder of Thinktank Avenir Swiss, and the presentations of current CTI life sciences projects and their strategic role for the industry and academic partners, as well as the poster exhibition in the networking area.

During the Basel Life Science Week from 19 - 23 September 2016, four international speakers presented their topics on the theme of "Molecular Diagnostics brought by NTN Swiss Biotech™.

In a world of dwindling fossil-based energy, global air pollution and warming, biocatalysis may be a perfect problem solver. It has the potential to deliver sustainable raw materials and energy from biomass, and enables chiral and highly functionalized compounds to be produced ecologically for the chemical and pharmaceutical industry. At ZHAW Life Sciences and Facility Management on 20 June, the Competence Center for Biocatalysis (CCBIO) headed by Dr. Rebecca Buller, gave European experts the opportunity to present the latest findings from science, research and practice in the future oriented field of biocatalysis.

Life long learning and formation of the next generation
In response to current needs for advanced professional training, Roche offers its employees an intensive course in cell cultivation and downstreaming under the auspices of biotechnet Switzerland. In 2016, lecturers from the ZHAW, Life Sciences and Facility Management gave participants the benefit of their expertise in theory and laboratory practice. One valuable side effect is the creation of a permanent network of specialists.

11th Summer School on Advance Biotechnology
The 11th biotechnet Summer School on Advanced Biotechnology 2016 was held in the Orto Botanico of the University of Palermo. Students (bachelor, master and PhD), researchers and teachers from Italy, Switzerland and Austria met to discuss important topics of biotechnology.

Platform events organized or co-organized by NTN Swiss Biotech™
Visit of the Clinical Chemistry Laboratories of the Inselspital Bern, 25 April 2016, Bern
Industrial Biocatalysis: 8th Wädenswil Day of Life Science, 20 June 2016, Wädenswil
Second Antibiotics Platform meeting, 20 June 2016
Polyphor Ltd., Allschwil
Latsis Symposium ETH Zurich on Personalized Medicine, 29 June 2016, Zurich
Retreat Competence Center-Personalized Medicine, 30 October 2016, Kartause Ittingen

The comprehensive program of activities by NTN Swiss Biotech™ and its partners biotechnet and Swiss Biotech Association has been recognized with funding by the CTI KTT program until end of 2018.

Since 2013 the National Thematic Network Swiss Biotech™, led by biotechnet Switzerland and the Swiss Biotech Association, has made it a goal to foster transfer activities in biotechnology.

The Swiss Biotech Association (SBA), founded in March 1998, is the national industry association of small and medium-sized enterprises active in all areas or biotechnology. It has some 200 member companies and is a highly respected networking platform. For further information visit www.swissbiotech.org.

biotechnet Switzerland is the network of Swiss and Austrian Universities of Applied Sciences (FHNW, HES-SO, ZHAW, MCI), the research institution CSEM, the Swiss Center for Regenerative Medicine at the University Hospital and University Zurich and the Competence Center Personalized Medicine UZH/ETH. The biotechnet Switzerland is the one-stop shop for innovation in technology where companies, especially small and medium-sized ones, can easily access relevant specialists for their development work. For further information visit www.biotechnet.ch.
From CTI to Innosuisse

The Commission of Technology and Innovation (CTI) is the Swiss Confederation’s innovation promotion agency. It provides consultancy and networking services and financial resources to help turn scientific research into economic results. From 1 January 2018, Innosuisse will take over the functions of the current CTI.

In June 2016, the Swiss Parliament approved the Swiss Innovation Promotion Agency, or Innosuisse Act. The Innosuisse Act provides the legal basis for the CTI to become an institution under public law. On 9 December 2016, the Federal Council appointed the Innosuisse Board made up of seven specialists from the realms of science and business. This board will play a key role in Innosuisse’s success.

The Federal Council appointed André Kudelski, Président Directeur Général (CEO) of Kudelski Group in Cheseaux-sur-Lausanne, as President of the Innosuisse Board. Further members of the board are:

– Prof. Edouard Bugnion, Professor at the EPFL, Laboratoire de Théorie de l’Information in Lausanne
– Dr. Thierry Calame, Partner and Co-Head of the Intellectual Property Expert Group at Lenz & Staehelin in Zurich
– Trudi Haemmerli, CEO and Director of UK-based PerioC and Managing Director of TruStep Consulting in Basel
– Prof. Martina Hirayama, Director of the School of Engineering, Zurich University of Applied Sciences in Winterthur
– Marco Illy, Managing Director and Head of Swiss Investment Banking at Crédit Suisse in Zurich
– Nicola Thibaudeau, CEO of MPS Micro Precision System in Bienne

The Federal Council selected the board members on the basis of a requirement profile drawn up by the Federal Department of Economic Affairs, Education and Research (EAER). The newly appointed board is tasked with setting up Innosuisse to begin operations by the end of 2017, and with creating a sound basis for the agency’s future activities.

The board’s tasks include issuing Innosuisse’s organizational regulations and ordinances and approving a multi-year program, budget and annual report. The board also decides on appointments to the management team of the Innosuisse Secretariat, appoints members of the Innovation Council, and is responsible for overseeing these bodies. Furthermore, it is responsible for implementing and reporting on the Federal Council’s strategic objectives.

CTI Special Measures 2016

The 2016 CTI Special Measures to mitigate the effects of the strong Swiss franc, put in place by the CTI on behalf of the Federal Council and Parliament, have now come to an end. Under these measures, in addition to the regular CTI funding, 161 special innovation projects out of 335 applications involving export-oriented small and medium-sized enterprises (SMEs) were approved in the period July to December 2016 (approval rate around 48%). These projects received a total funding of CHF 60.3 million.

The facilitated conditions of the CTI Special Measures (i.e. the reduction of cash contribution from business partners and the reduction of the minimal own contribution of the business partners from 50% to 30%) were welcomed by Swiss SMEs. SMEs were also keen to make use of the CTI’s Innovation Mentors, who advised and supported the companies with their project applications.

The CTI Special Measures federal funds were distributed across the CTI’s funding areas as follows:

– Engineering Sciences: CHF 24.0 million for 68 projects
– Micro- and Nanotechnologies: CHF 17.0 million for 42 projects
– Enabling Sciences: CHF 7.0 million for 22 projects
– Life Sciences: CHF 12.3 million for 29 projects

New funding instrument BRIDGE

The Swiss National Science Foundation (SNSF) and the CTI have jointly set up the new program BRIDGE to complement the support they already provide for Swiss science and innovation. BRIDGE aims to better exploit the economic and societal potential of scientific research by promoting the transfer from scientific knowledge to innovation.

BRIDGE will facilitate cooperation between universities, the Swiss Federal Institutes of Technology, research institutes and universities of applied sciences. Two funding types are implemented:

– Proof of Concept: 12 to 18 months funding for young researchers.
– Discovery: up to four years funding for experienced researchers, either as individuals or in a consortium

CTI’s international activities

The CTI acts as the Swiss funding organization for innovation-oriented, bilateral or multilateral, international or European R&D cooperation programs. Despite the fact that the legal status of Switzerland in EU research programs was unclear throughout 2016, the CTI continued its efforts to secure the participation of Swiss scientists and companies in ERA Cofund activities. Happily, Switzerland’s status as a fully associated country within Horizon 2020 was confirmed as of 1 January, 2017.
Within life sciences the main focus for the CTI ERA-Net activities was the participation in the ERA-Net CoFund on Biotechnologies (ERA CoBioTech). The first call for ERA CoBioTech projects was announced on 1 December 2016. 18 funding organizations from 18 countries are involved in this call with a total available budget of EUR 36 million. The deadline for preproposals was 2 March 2017 and for full proposals 20 July 2017.

Following the first and second successful calls in 2015 and 2016, the Korea Institute for Advancement of Technology (KIAT) and CTI launched a third call for joint innovation projects between Switzerland and South Korea on 8 March 2017. The call covered biotechnology, medtech and ICT. The aim is to encourage companies and research institutions to carry out joint science-based innovation projects that benefit both countries. It is targeted at Swiss and South Korean companies which recognize the two countries as major markets and research locations and are interested in taking advantage of the KIAT and CTI joint funding programme.

CCOS – success based on collaboration
The idea of creating a national culture collection for Switzerland popped up around 2007. It was triggered by national need and supported by several groups of stakeholders such as the Swiss Industrial Biocatalysis Consortium (SIBC), the Swiss Academy of Technical Sciences (SATW), the Swiss Biotech Association (SBA) and the biotechnet Switzerland.

The joint efforts led to a CTI-funded project running from 2009 to 2011 with the Zurich University of Applied Sciences in Wädenswil (led by Prof. Martin Sievers and Dr. Gottfried Dasen) as the research partner and SBA representing the Swiss biotech industry. Additional funding from the Federal Office of the Environment (FOEN) was granted to cover biodiversity aspects.

As a result of the CTI project, the Culture Collection of Switzerland (CCOS), located in Wädenswil, was registered as a limited liability company in 2010. The CCOS is now the official national collection of microorganisms in Switzerland. It plays a major role in dealing with Switzerland’s obligations towards the implementation of the Biodiversity Convention and the Nagoya Protocol. It offers secure storage bank services for microbial strains, animal and human cell cultures and other samples of biological origin.

Today, CCOS is a member of the World Federation of Culture Collections (WFCC) and a member of the European Culture Collections Organization (ECCO). In addition, the CCOS is ISO 9001 certified and now manages more than 2500 strains.


The Culture Collection of Switzerland (CCOS)

The Culture Collection of Switzerland (CCOS) is the Swiss national public culture collection for microorganisms and supports the life sciences community with biological material, cryostorage and services. Choose the field of your interest and learn more about it!

Biosources
Find biological resources from bacteria to cell cultures for your application.

Bio Storage
Store a backup or make a Patent Deposit of your biological resources at our secure facility in Switzerland.

Bio Services
Explore our laboratory and analysis services to facilitate your processes.

Source: www.ccos.ch
Freedom-to-operate in biotech: multiplied complexities

Over the past two decades, the biotech industry has matured into an established business with numerous commercial products generating high returns on investment. In parallel, novel technologies, new players and additional fields of application have continued to increase overall diversity. All along, patents have been instrumental in protecting products and encouraging investment in this high risk/high potential industry. Consequently, the patent landscape for biotechnology has become large and complex.

Diverse and dense patent thicket

The number of biotech patents is increasing rapidly and continuously. In 2016, the total number of active patents exceeded 250,000, with China replacing the USA as the number 1 country of origin and Switzerland remaining in 11th place (figure below left).

It is worth noting that among the top 13 countries, the patents of Danish and of Swiss origin are located in the ‘sweet spot’ of the patent landscape (figure below right). This is due to their high Technology Relevance™ combined with a broad Market Coverage™, two parameters further explained in the note below the graphs.

The steady increase in the number of biotech patents results from growth in multiple dimensions: higher density in established fields, expansion to novel areas, and combination of technologies.

– The density of patents has become extremely high in established fields of biotechnology, such as health, chemistry, measurements, and agriculture. Nevertheless, emerging technologies, innovative combinations and improved, known features enable further developments and generate novel, patentable products and processes. Therefore, it is safe to assume that the patent density in the classical biotechnology fields will further increase in the future.

– Biotechnology continues to expand into novel, so far unexplored fields of application. As a result, the overall number of patents is increasing and alongside it, the diversity of the biotechnology patent landscape.

– The combination of biotech with other emerging technologies, for example digital technology or additive manufacturing, is bound to generate entirely novel product and process categories. Such combinations are prone to generate highly complex patents and involving multiple scientific disciplines.

Note: The figures above are based on a collection of over 500,000 biotech patent families selected in accordance with the OECD definition of biotechnology (https://www.oecd.org/sti/sci-tech/34935605.pdf, table 5, p32). Both graphs were generated with the patent analysis software PatentSight (www.patentsight.com). The origin of an invention is defined by the country of residence of the inventors. The parameters – Technology Relevance™ and Market Coverage™ – for a given patent family are calculated by PatentSight from the frequency of citation and the country coverage, respectively. For both parameters, the value 1 represents the reference value, i.e. the average of all patents.
Freedom-to-operate in biotechnology

The market launch of a new product initiates its commercial exploitation after a long period of product development and substantial investment. A worst-case scenario at this point is an unexpected infringement action filed by a competitor. Freedom-to-operate (FTO) analyses serve to avoid this scenario and to evaluate the risks of infringing existing or pending patents for a defined product or process in specified markets at a given time.

It is worth noting that the fact that a company owns patents protecting a new product, does not preclude the risk of infringing patents of third parties. Own patents may depend on earlier, broader patents owned by third parties, or they may not cover all relevant aspects of a given product. The objective of an FTO analysis is a near complete account of potentially infringed patents for a defined product or process. Thus, the effort needed to avoid infringement increases with the complexity of the investigated subject matter. FTO analyses relating to biotechnology are particularly intricate because several complexity factors coincide and multiply.

As outlined above, the increasingly dense and diverse biotechnology patent landscape represents a patent thicket, which is difficult to navigate. Patent thickets also exist in other domains, such as telecom, but in biotechnology, additional factors render the FTO task particularly challenging.

– The involvement of living organisms makes biotechnology patents inherently complex, in particular those involving biological processes. Even in its simplest forms, life comprises countless interconnected mechanisms and a high degree of redundancy and variability. As a result, the scope of protection of biotechnology patents is frequently fuzzy due to poorly defined or implicit features.

– Many technical terms used in life sciences are ambiguous or even controversial, and multiple synonyms describe the same subject. These linguistic hurdles impede the analysis of both patents and scientific literature, and they add one more layer of complexity.

– Many biotechnology products target a global market. Accordingly, FTO has to consider multiple countries, each with specific competitors, IP-legislations, and patent landscapes. For obvious reasons, this aspect broadens the scope of any FTO analysis.

Obtaining a realistic view of the FTO situation for a biotechnology product or process means managing the multiplied complexities involved. A systematic, stepwise approach helps to structure and focus the task, and support from IP professionals with specific knowledge of biotechnology is necessary.

Ideally, FTO accompanies the entire product development process, as an integral part of a comprehensive risk management. From early stages onwards, FTO aspects can significantly influence key decisions and help to prevent dead-end developments or costly redesigns at late stages.

Early on, the FTO may focus on a few key features of the envisaged product, and on a tightly defined core market. In parallel with the progress of the project and with increasingly precise product specifications, the FTO analysis can become progressively thorough by addressing more features and a broader market. This approach ensures a reliable, comprehensive FTO assessment up to and beyond market entry. In addition, the stepwise process can provide valuable insights into the dynamics of the technologies, players, and markets involved.

In summary, FTO analyses in biotechnology are a particular challenge due to multiplied complexities. FTO in biotechnology means having to address many difficult-to-define features within a dense, diverse, and highly dynamic patent landscape at a global level. However, the objective can be achieved by addressing FTO early on with an incremental approach and professional support, but most of all by ensuring a high IP-awareness of both scientists and decision makers in the industry.

Assisted Patent Landscape Analysis by the IPI

With an Assisted Patent Landscape Analysis, you can obtain valuable information about your technology sector and your competitors within a day. Together with an expert from the Swiss Institute of Intellectual Property (IPI), you first identify a core set of relevant patent documents from your technology sector. You then analyse the data together and uncover the connections between them using suitable tools and analysis techniques.
Switzerland, a great environment for complex industries

Switzerland offers good framework conditions for complex industries. One example is the highly specialized flavour and fragrance sector, in which Swiss companies occupy a world leadership role. For them, biotechnology plays an increasingly important role, as it does for the chemistry, healthcare and life sciences sector in general.

An early-morning walk in a damp spring forest when the first rays of sunlight touch the ground, a visit to a crowded oriental market overflowing with goods, spices and colors; an exquisite candle-light dinner accompanied by a selection of elegant wines: olfactory sensations are important components of how we perceive the world around us. They are deeply connected to our emotions and inseparably interwoven with our memories.

The perception of smells and flavours is a highly complex process, and scientists have estimated that humans can distinguish more than 1 trillion \((10^{12})\) olfactory stimuli. Chemical analysis has detected about 500 volatile molecules that contribute to the aroma and bouquet of wine, but mere scientific analysis does not diminish the wonder at the enormous complexity of our sense of smell and how it contributes to our quality of life.

**Complexity in flavours and fragrances**

The flavour and fragrance industry provides key ingredients for food, drink, home and personal care products and accordingly has a highly complex structure. A huge range of raw materials, with different supply chains, is sourced from all over the world. Production processes, ranging from traditional extractions through synthesis by green chemistry to modern biotech approaches, have to be coordinated and integrated.

Demands and expectations of customers in a global market place vary widely according to local tastes and customs. This makes it necessary to offer a wide range of products with finely tuned sensory properties. Research and development requires the global collection of samples and ideas, and the analysis and integration of huge amounts of biological, chemical, physical and sensory data.

A fine balance between tradition and highly innovative approaches is required to support established products and bring new ones to the market. Biotechnology plays an increasingly important role in the flavour and fragrance industry, helping to secure reliable and sustainable provision of key ingredients and to gain access to compounds with new properties as the basis for novel products.

**Swiss companies lead the way**

Givaudan and Firmenich, the two largest players in the flavour and fragrance ingredients market have their headquarters in Switzerland. Together, they capture about one third of the global fragrance and flavour ingredients market that in 2016 was estimated to have a total combined value of USD 26.5 billion and growing strongly.

For both companies, biotechnology plays an increasingly important role in both R&D and production. In 2016, Firmenich announced the large-scale production of AMBROX®, an amber fragrance with musk and wood tonalities using a breakthrough white biotechnology fermentation process, coupled with proprietary green chemistry. Just the year before, the company won the prestigious Sepawa Innovation Award for its CLEARWOOD® perfume ingredient. With woody and patchouli notes, this ingredient is produced by a sustainable process based on Firmenich’s industrial (white) biotechnology platform.

For Givaudan too, industrial biotechnology offers a multitude of opportunities to the flavour and fragrance sector. The company expects that eventually about half of the fragrance compounds will be produced using biotechnology and it is actively engaging in research and collaborations in this field.

It is not only the economic potential, but also the possibility of increasing the sustainability of production processes that is an important success factor. For example, a research and production facility integrated into the Bazancourt-Pomacle biorefinery in northeast France is transforming the way the company produces cosmetic ingredients. The circular economy model contributes to a positive growth dynamic, while helping to achieve Givaudan’s eco-efficiency targets.

**Success factors in Switzerland**

It is probably no coincidence that Switzerland, long known for a watchmaking tradition that requires a mastery of complexity and a fine hand for details, is also a place where these leaders from the flavour and fragrance sector can thrive. Switzerland regularly occupies top rankings in global innovation. The comprehensive education system provides a motivated workforce at different qualification levels and the high standard of living in Switzerland makes it easy to attract top talent from abroad.

Publicly funded education and research institutions are well equipped, internationally connected, and draw top scientists from all over the world. The research landscape stretches from academia, through innovative start-ups and SMEs, and on to large, multinational companies with their global resources. Efficient knowledge and technology transfer between basic and applied research and industrial applications further stimulates innovation.
scienceindustries supports some 250 member companies by fostering an innovation-friendly environment in Switzerland, a competitive production and business framework, attractive market conditions and by facilitating worldwide market access. For more information visit www.scienceindustries.ch.

The biotechnology sector also benefits from Switzerland’s research and knowledge infrastructure such as the Competence Center for Biocatalysis CCBIO at the Zurich University of Applied Sciences (ZHAW), and the well-established precompetitive collaboration between key players within the Swiss Industrial Biocatalysis Consortium (SIBC).

Switzerland’s leading exporter

The chemistry, pharma and biotech sector share of total Swiss exports has been steadily increasing over the years, from 31.8% in 2001 to 44.8% in 2016. Since 2009, the sector, which is represented by scienceindustries, the Swiss association of the chemistry, pharma and biotech industry, has become the largest export industry in Switzerland. In 2016, its exports reached CHF 94.3 billion – a new record. About CHF 80.3 billion was contributed by exports of pharmaceutical products, where biotechnology plays a major role.

The diversity of the product portfolio in the sector and the clear focus on life sciences is reflected in a further breakdown of the export statistics. Besides pharmaceuticals, vitamins and diagnostics, that together make up the lion’s share of 85%, it ranges through fine chemicals, agribusiness, plastics, flavours and fragrances, and pigments (see figure below).

The Swiss chemistry, pharma and biotech sector has a decidedly international orientation, which is clearly demonstrated by the geographical breakdown of global sales. For the top ten scienceindustries member companies, the total turnover of CHF 137.6 billion in 2015 was achieved mostly in the Americas, other European countries and Asia, with only a very small proportion in the domestic market (see figure above).

World-wide marketing based on the manufacturing and sale of innovative high-value products, is an essential part of the strategy of scienceindustries member companies. Swiss companies, not only the big multinational corporations but also many small and medium-sized enterprises which pursue their successful niche strategies, have been present on international markets for decades.

Swiss export statistics according to industry sector demonstrate the lead of the chemistry, pharma and biotech industry (scienceindustries/Federal Customs Administration 2017)
Switzerland: success through diversity

For many years, Switzerland has held the top spot in one of the best known international competitiveness indexes. In 2016, for the eighth consecutive year, it took first place in the World Economic Forum (WEF) annual rankings. With an average USD 81,324, Switzerland’s per capita gross domestic product is the fourth largest in the world.

Compared to other countries, Switzerland maintains relatively high levels of Foreign Direct Investment (FDI). In 2016, FDI in Switzerland amounted to USD 750 billion. From a historical perspective, the importance of foreign investment is clear, with Swiss capital invested abroad almost triple what it was in 2000. What is the story behind these numbers? Why has Switzerland become such a special place for business and innovation? After all, it is only a very small country with a commensurately small population. And there are hardly any natural resources that would make a substantial contribution to national wealth.

Switzerland has four national languages and 26 different cantons, each with its own individual authority in key areas of government such as tax, education and energy. At a national level there are seven Federal Councillors who work in an annual presidency based on a rotational system. A decision can only be made when a consensus is reached. But important decisions in a direct democracy such as Switzerland’s, tend to be made by the Swiss citizens themselves. The Swiss governmental system is built on the principle of federalism and subsidiarity; the Swiss only want the authorities to be involved when necessary. Responsibility and initiative are highly valued.

It is fair to say that Switzerland operates a complex political system where many players have considerable authority to decide and define solutions to problems. This means that in daily life, diversity of opinions and solutions is high. The result is that the best solution tends to come out ahead of weaker ones and serves as a model of best practice going forward.

These days, diversity is considered a major driver of innovation. It has been proven that diverse teams perform better and are more innovative than others. According to a new report from Times Higher Education, the top two ‘most international universities’ are in Switzerland and they also rank amongst the top performing universities worldwide. It is the international make-up of research teams that delivers the remarkable innovation capacity that we find in Switzerland. Maybe it is that only these factors have made Switzerland exceptional. Other than brains and ideas, business and trade, there is not much else in terms of resources to rely on. So the Swiss have developed an economic and social system that is built on the four pillars of innovation, technology, security and trust; thus creating a national spirit that embraces diversity to deliver innovation, performance and quality.

Switzerland provides a fertile ground for new ideas – in no other country are newly developed technologies and inventions better protected than in Switzerland. Additional assets include a healthy capital market, a broad offering of financial and insurance products and services, as well as long term economic and monetary stability. Over the last 150 years, the Swiss political system has proven to be exceptionally stable and reliable – and so has the social environment and the Swiss currency. Low inflation rates, low capital costs, a good investment climate and solid purchasing power make the Swiss economy one of the most liberal and competitive in the world. The country’s gross domestic product is considerably higher than the EU average.

Foreign workers and companies value the international outlook of the Swiss. Additional assets are personal freedom, an extremely well-preserved natural environment with clean lakes and rivers, and a well-developed infrastructure. The Swiss healthcare system is one of the best in the world.

These characteristics have helped Switzerland become a leading center for many industry sectors; this simplifies networking, partnering and access to new markets for investors. The Swiss have found a way to combine innovation and stability, security and confidence, performance and quality of life. The roots of the country – history, mentality, and heritage – go deep and feed the pillars that make Switzerland a great place for investors and also as one of the best places to live in the world.

Switzerland Global Enterprise (S-GE) works all over the world to support entrepreneurs and promote Switzerland as a business location. In its role as a center of excellence for internationalization the agency’s mission is to foster exports, imports and investments, to help clients develop new potential for their international businesses and to strengthen Switzerland as an economic hub. S-GE, with a global network of experienced advisers and experts, is a strong and trusted partner for its clients, the cantons and the Swiss government. For further information visit www.s-ge.com, www.s-ge.com/handbookforinvestors, www.s-ge.com/invest-biotech, www.s-ge.com/innovation, www.s-ge.com/company-foundation.
Reducing complexity as a function of strategy

Roundtable moderators:

Andrea von Bartenwerffler,
Head Account Management,
Issuer Relations, SIX Swiss Exchange AG

Christian Geiger,
Relationship Manager,
Issuer Relations, SIX Swiss Exchange AG

The call for clarity has never been louder because it is considered essential when it comes to making sense of complexity. Companies that master a structured approach to reduce complexity will unlock new opportunities and successfully manage the ever-growing list of regulations. Not only will they become more effective, they will also be better understood by the public and investors. SIX solicits the view of executives from listed companies and a corporate finance representative.

Roundtable participants:

Ronald Scott,
CEO, Basilea Pharmaceutica (SIX: BSLN)

Dr. Chris Tanner,
Head of Transactions Office and Head of Investor Relations, Cosmo Pharmaceuticals (SIX: COPN)

Stefan Weber,
CEO, Newron (SIX: NWRN)

Marc Klingelfuss,
Managing Director, Deputy Head of Corporate Finance, Bank Vontobel

SIX: What does complexity mean to your company?

Scott: Basilea is in the middle of rolling out two novel, innovative hospital products around the world. In key European markets, we are directly leading this project. There, the country-specific pricing and reimbursement structures and processes, with their national, regional and even local levels, add another level of complexity to market access as compared to the single US market.

Regarding innovation, the development of new therapies for unmet medical needs in areas such as oncology and hospital anti-infectives, frequently requires the combining of different products. This increases the complexity in drug discovery and development but also provides opportunities, especially for smaller, fast-moving and flexible companies such as our own that have the relevant know-how.

Tanner: For Cosmo, complexity starts with every new employee. Hiring and retaining the right breed of employees is a major task for us as their integration potentially reduces or increases the complexity of our organization. Most of these specialists come from big pharma companies. The challenge is to balance the need to nurture the existing culture and the entrepreneurial spirit of the early days with the need to add new expertise as we grow into a full-scale company with processes in place for every task.

Weber: Newron develops innovative therapies for disorders of the central nervous system. Strategically, we focus our activities around both, the ‘R’ and the ‘D’ of R&D as well as the commercialization of drugs for rare diseases. So, we do not care ourselves for research or production, nor do we build in-house capacities for all disciplines in development such as pharmacology or toxicology. We fare better when we contract the best specialists and pay them by the hour. In our experience, the flexibility we gain is worth more than the associated risks and costs.

SIX: What areas currently pose the most complex challenges for your company?

Tanner: Cosmo’s strategy is to build an integrated company that covers all aspects of drug development, production and commercialization. Experience taught us that dealing with these complexities internally is the best option for us. In the past, we partnered the development and commercial rights, thereby delegating the complexity, but we became dependent on our partners’ commitment and capacity to master it.

Partnering means that you take an extremely complex decision now in the hope that it will turn out to be the right decision in the long run. We decided to go all the way by ourselves and add complexity step by step as we constantly learn and adapt to new challenges.

Weber: Newron focuses on orphan indications for three reasons: first, we only need one single pivotal trial for market approval; second, once approved, we can commercialize the products by our own organization; third, in the orphan space, you don’t need a huge sales force to serve the markets.

If everything goes according to plan, we start shipping our first orphan product in Rett syndrome by the end of 2018 or early 2019. Our current prediction is that a specialized sales team of 25 to 35 medical liaison officers will suffice to do this in Europe and North America. However, making marketing and sales a core competence will put our ability to adapt and overcome new challenges to the test.

Scott: A current key focus for Basilea is to ensure that patients, who are outside our core European markets and the USA and in need of novel therapies, can gain access to our products as quickly as possible. There are different regulatory and legal requirements for the registration and commercialization of
drugs in each country. In order to effectively and efficiently access all of these markets, a local presence is required. In certain countries this may be mandatory in order to register and commercialize drugs.

**SIX: How do you reduce complexity in these areas and prevent complexity in others?**

*Weber:* With a staff of 24 employees, Newron has to stick to its core competences and source the rest. There is no reason why we should abandon this approach in the future even as we grow into a commercial company. We reduce complexity by focusing on key areas and become masters in whatever we do. Everything else is outsourced to partners with the expertise and a track record in a given specialty task. Our main challenge is to manage these interfaces. That’s why project and relationship management is one of our core competences.

*Scott:* Basilea is working with a contract sales organization for our approved products in the core European markets. This allows us to leverage existing infrastructure without the need for us to expand our own infrastructure. In regions like Latin America, the Middle East and North Africa, we entered into partnerships with specialized regional partners who have an understanding of local regulations. They manage the registration process and the commercialization, which significantly reduces complexity on our side.

Another example of how we address the economic complexity is our contract with the US Biomedical Advanced Research and Development Authority (BARDA), under which we receive government funding for the phase III development of our antibiotic Cefotibipro in the US. In oncology, we follow yet another approach to reduce complexity. We plan to partner our drug candidates in mid-to late stage development to specialists with the expertise to run global clinical studies in multiple tumor types. Focus is key in a highly regulated industry. It is critical to focus on one’s strengths and to establish a structure that allows organizations to deliver value-driving milestones.

*Tanner:* Retaining full control over our assets is a cornerstone of Cosmo’s strategy. We accept the associated increase in complexity as a trade-off. In 2012, we partnered our candidates in dermatology with a US company. We gained some financial flexibility and focused on the gastro-intestinal pipeline. However, two years later we terminated the collaboration.

Instead of re-integrating the dermatological business, we decided to transfer all assets into a separate, albeit fully-owned entity. The main reason was to reduce the complexities of running a company with two different pillars that had only little synergy but lots of differences such as markets, culture and people. In 2015, we took this separate company public under the name Cassiopea.

**SIX: Complexity and growth seem to be twins, particularly in the biopharmaceutical industry. Is complexity an inevitable companion of growth?**

*Scott:* Innovations that translate into improved treatments for patients, for instance in the oncology field, keep on raising the bar for providing significant medical benefits, preferably in a targeted fashion or ideally as personalized medicine. However, in many medical areas, the required combination of complementary treatment approaches to further improve patient outcome is adding complexity. On the other hand, our understanding of biology keeps on increasing and we thus have access to more tools to address the problem. This is why there are increasingly more R&D partnerships established even among the big pharmaceutical companies.

*Weber:* We opportunistically focus on our sub-class of non-toxic voltage gated sodium channel blockers and our expertise in reprofiling compounds in orphan indications. The group of ion channel blockers was originally discovered by our founders, and by repurposing them into indications other than epilepsy, we have managed to present unique mechanisms of action in Parkinson’s disease, schizophrenia and pain indications.

The second pillar is the ‘in-licensing’ of compounds with a proven toxicity and safety. Sarizotan is such an example. Originally developed for Parkinson’s disease, we now develop the compound in Rett syndrome, a rare debilitating genetic disorder of the brain. Because Sarizotan is safe, we can focus on efficacy and this saves money and time.

*Tanner:* Growth results in larger organizations and larger organizations require a division of labor to remain effective. The downside is that collaboration becomes more complex as frictions occur more frequently. In our industry, complexity increases exponentially if a company decides to build its own integrated biopharmaceutical business.

Most biotechs start with some research labs and a first major crossroad comes when a compound is ready to enter the clinic. Retaining an external CRO (contract research organization) or building your own development team has a tremendous impact on the complexity. The commercialization of a compound represents another major threshold: build your own sales force or partner the rights.

*Klingelfuss:* No doubt, the life science industry is extremely complex as it deals with life itself in its countless variations. Even for a non-industry practitioner it is clear that every aspect of drug development, production and commercialization is heavily regulated with more legislation looming. In this context growth can imply further complexity and there are many different ways to manage it effectively. There seems to be no one-size-fits-it-all solution to reduce complexity. The approaches...
companies opt for are rather a reflection of their strategy, people and resources.

The complexities of raising capital for growth can also be addressed through different sources: going public is just one of the alternatives available to biotech companies. They are used to dealing with complexity and operating within a regulated environment, which facilitates the adoption of the additional requirements that go with becoming a listed company. With regard to minimizing complexity, SIX Swiss Exchange offers a straightforward regulatory framework, helping companies to become and stay public with as little effort as possible.

**SIX**: The preparation for an IPO is considered to be a first major exercise to reduce complexity. What was your experience?

**Weber**: Who wouldn’t agree that housekeeping is a permanent task? In practice, urgent matters and daily routine tend to stimulate quick solutions. This holds true for Newron, too. In the run up to our going public, we abolished the organically grown structures and replaced habit with written processes. We abandoned the different classes of shares, introduced formal checks and balances and much more. The effort was well worth it and resulted in a lean, transparent and hence more efficient company.

**Tanner**: The first clean-up campaign at Cosmo was undertaken when professional investors came on board. The IPO brought additional tasks particularly in public reporting. The pressure to explain our business and how our activities fit into the strategy, results in the continuous re-evaluation of certain projects, in particular non-core activities with no near-term inflection points. The spin-off Dermatos, which we IPO’ed in 2015 at SIX Swiss Exchange under the new name Cassiopea, is the result of such considerations.

**Scott**: Basilea went public in Switzerland back in 2004. The listing requirements and reporting obligations have been evolving in the interest of increasing transparency – which is good for companies and investors. As an issuer, the existence of a critical mass of peer companies on the listing platform is helpful, as it typically leads to investors being more familiar and comfortable with the complexity entailed in the biopharmaceutical business.

**Klingelfuss**: When preparing for an IPO, the task of phrasing an attractive and compelling investment case for sector-specialist as well as generalist investors forces the organization to find ways to reduce the complexity. When the management team phrases its equity story, it has to focus on key messages relevant to potential investors and their investment decision. At this stage it becomes clear that it needs to take into account that the focus of specialist and generalist investors differs.

**SIX**: Some say a transatlantic listing might offer many opportunities. However, this comes with a significant increase in complexity. What is your view?

**Tanner**: A listing on a foreign exchange, and in particular in the USA, results in a significant increase in regulatory and reporting complexities. Companies need additional staff for financial reporting and permanent legal assistance from external lawyers. In my view, such a listing abroad can easily turn into a risky and expensive endeavor.

Every company is different and so is their appetite for risks. For some, the larger pool of institutional investors might justify a listing in the USA. Also, US investors are usually more open and risk seeking. For Cosmo and Cassiopea, the pros and cons remain in favor of a SIX listing and I don’t expect this will change in the near future.

**Scott**: It is true that a transatlantic or even dual listing may add complexity. For instance through different or additional reporting obligations, overlapping and longer trading hours or different liquidity on the different trading platforms. This would have to be appropriately managed and requires employees in the US. On the other hand, there may also be benefits related to such a listing, in particular for companies in our industry. These may include enhanced visibility and analyst coverage, increased liquidity, a larger number of peers, and access to capital to fund growth.

**Weber**: The question is how to attract US investors by becoming relevant money-wise, since they are key for a higher market capitalization for every biotech company. An estimated two thirds of investments originate in the USA and approximately half of these are available for overseas investment targets.

When Newron prepared for the IPO, the odds for success were clearly in favor of the SIX. However, there is no guarantee for a steady flow of US funds for European biotech companies. That is why we regularly weigh the costs of financial reporting and regulatory compliance versus the benefits of access to the largest investment pool in our industry.

**Klingelfuss**: A number of European biotech companies, including a few Swiss ones, have considered a listing overseas. This is not a new trend. In the USA, there is a considerably larger pool of specialist investors with a bigger risk appetite for early stage biotech companies than in Europe. However, there is also a much larger number of listed biotech companies available to these specialist US investors. They tend to vote with their feet if the performance of the company does not meet their high expectations.
It is important to note that many institutional US investors can also invest in an IPO on SIX Swiss Exchange, if the offering includes a private placement under Rule 144A of the US Securities Act. Adding such a 144A tranche will incur additional, though limited, costs and preparation work for the company.

There are additional incentives for early stage biotech companies to list in the USA like the 2012 JOBS (Jumpstart Our Business Startups) Act. But as going public has a long-lasting impact, it is well worth looking at the increase in complexity that a European company faces in the USA. Sooner or later, companies need to be compliant with Sarbanes-Oxley, meaning that, when they reach a certain market cap or maturity, the more complex US regulations will need to be fulfilled.

In certain cases extra staff, designated to the US market, will be required. Overall a transatlantic listing brings more complexity that needs to be properly assessed.

SIX Swiss Exchange listed life science companies outperform their peers

SIX Life Science Indices performance comparison

SIX Swiss Exchange
SIX Swiss Exchange is one of the leading exchanges in Europe and an ideal listing location for companies of every origin, size and sector. Listed companies benefit from access to experienced, highly capitalized international investors and high liquidity. Thanks to our excellent networking and personal support we offer them an efficient capital-raising. We maintain a close dialogue with both our domestic and foreign customers, working intensively with them to create optimal conditions for their success. For further information visit www.six-swiss-exchange.com

The roundtable was organized by Thomas Staffelbach of TS Kommunikation, a specialized PR and IR consultancy for biotech companies.
Year in review: selection of events in 2016

<table>
<thead>
<tr>
<th>Trigger</th>
<th>Company/Institution</th>
<th>Description</th>
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<tbody>
<tr>
<td><strong>January 2016</strong></td>
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<tr>
<td>Orphan Drug Designation</td>
<td>Addex Therapeutics (ADXN)</td>
<td>Addex’ Dipraglurant received Orphan Drug Designation from the FDA for Levodopa-Induced Dyskinesia associated with Parkinson’s Disease.</td>
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<td>Clinical development</td>
<td>Molecular Partners (MOLN)</td>
<td>Molecular Partners to conduct phase II trial of MP0250, a multi-DARPin targeting VEGF and HGF, in multiple myeloma.</td>
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<tr>
<td>Financing</td>
<td>Cardiorentis</td>
<td>Cardiorentis raised CHF 60 million in series B financing and adds two key senior executives.</td>
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<tr>
<td>Financing</td>
<td>Novimmune</td>
<td>Novimmune announced it has completed a CHF 30 million (USD 29.8 million) funding round.</td>
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<tr>
<td>Marketing/Distribution agreement</td>
<td>Santhera Pharmaceuticals (SANN)</td>
<td>Santhera signed distribution and supply agreement for Raxone® with Ewopharma covering Eastern Europe and the Baltics.</td>
</tr>
<tr>
<td>Merger</td>
<td>Kuros Biosurgery</td>
<td>Kuros Biosurgery closed merger with Cytos Biotechnology which is renamed Kuros Biosciences.</td>
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<td>Agreement termination</td>
<td>Basilea Pharmaceutica (BSLN)</td>
<td>GSK informed Basilea that it had elected not to continue its US alitretinoin program.</td>
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<tr>
<td>Product approval</td>
<td>Actelion (ATLN)</td>
<td>Actelion received Health Canada approval for Upravi (selexipag) for the long-term treatment of pulmonary arterial hypertension.</td>
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<td><strong>February 2016</strong></td>
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<tr>
<td>Award</td>
<td>InterAx Biotech</td>
<td>InterAx won the Swiss UpStart Challenge in the category Technology and received CHF 20,000.</td>
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<td>Collaboration agreement</td>
<td>PIQUR Therapeutics</td>
<td>Eisai and PIQUR signed landmark collaboration agreement.</td>
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<td><strong>March 2016</strong></td>
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<tr>
<td>Milestone achievement</td>
<td>Evolva (EVE)</td>
<td>Evolva achieved milestones in flavour &amp; fragrance alliance with Takasago.</td>
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<td>Product launch</td>
<td>Basilea Pharmaceutica (BSLN)</td>
<td>Basilea launched antifungal CRESEMBA® (isavuconazole) in the United Kingdom.</td>
</tr>
<tr>
<td>Product launch</td>
<td>Basilea Pharmaceutica (BSLN)</td>
<td>Basilea launched antifungal CRESEMBA® (isavuconazole) in Germany.</td>
</tr>
<tr>
<td>Study results</td>
<td>Adex Therapeutics (ADXN)</td>
<td>Addex reported successful completion of an mGLu5 receptor occupancy study with Dipraglurant in healthy volunteers.</td>
</tr>
<tr>
<td>Patent application</td>
<td>Redbiotec</td>
<td>Redbiotec has filed patent applications covering its novel antigens against Herpes simplex viruses. Redbiotec expected first results from its ongoing in vitro and in vivo studies by Q2 2016.</td>
</tr>
<tr>
<td>Study results</td>
<td>Celgene International</td>
<td>Oral Ozanimod showed histologic improvements in patients with ulcerative colitis in the phase II TOUCHSTONE trial.</td>
</tr>
<tr>
<td>Product approval</td>
<td>Actelion (ATLN)</td>
<td>Actelion received approval for Upravi (selexipag) for the treatment of pulmonary arterial hypertension in Australia and New Zealand.</td>
</tr>
<tr>
<td>Fast Track Designation</td>
<td>Humabs BioMed</td>
<td>Humabs announced that a novel antibody developed using its proprietary Cellclone technology has received Fast Track Designation from the US Food and Drug Administration (FDA). The investigational human monoclonal antibody MEDI8852 is being clinically developed by MedImmune.</td>
</tr>
<tr>
<td>Award</td>
<td>Polyphor</td>
<td>Polyphor announced USD 3 million award from Cystic Fibrosis Foundation Therapeutics to advance the clinical development of POL6014.</td>
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<tr>
<td>Research agreement</td>
<td>Evolva (EVE)</td>
<td>Evolva expanded its nootkatone research with CDC to include mosquitoes that transmit Zika and other viruses.</td>
</tr>
<tr>
<td>Patient enrolment</td>
<td>Auris Medical</td>
<td>Auris completed enrolment of TACTT2 phase III trial of AM-101 in acute inner ear tinnitus.</td>
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<tr>
<td><strong>April 2016</strong></td>
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<tr>
<td>Product approval</td>
<td>Actelion (ATLN)</td>
<td>Positive CHMP opinion for Upravi (selexipag) for the long-term treatment of Pulmonary Arterial Hypertension readopted.</td>
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<tr>
<td>Financing</td>
<td>Amal Therapeutics</td>
<td>Amal raised CHF 3 million in a series A financing round led by Boehringer Ingelheim Venture Fund.</td>
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<td>Event Type</td>
<td>Company/Partner</td>
<td>Details</td>
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<tr>
<td>Collaboration agreement</td>
<td>MabQuest</td>
<td>Partnership with Cellectis SA to develop and commercialize mAbs against PD-1.</td>
</tr>
<tr>
<td>License agreement</td>
<td>Evolva (EVE)</td>
<td>Evolva signed a license agreement with the US Centers for Disease Control and Prevention (CDC) that grants Evolva the exclusive worldwide patent rights to develop and commercialise nootkatone.</td>
</tr>
<tr>
<td>Financing</td>
<td>Anergis</td>
<td>Anergis closed CHF 5 million financing round extension to conduct large-scale ATIBAR trial with ultra-fast allergy immunotherapy. AllerT.</td>
</tr>
<tr>
<td>Study results</td>
<td>MaxiVax</td>
<td>MaxiVAX announced promising results from its phase I anti-cancer clinical trial.</td>
</tr>
<tr>
<td>Preclinical study results</td>
<td>Mymetics (MYMX)</td>
<td>Mymetics announced successful preclinical results with malaria transmission-blocking vaccine candidate.</td>
</tr>
<tr>
<td>Collaboration agreement</td>
<td>ADC Therapeutics</td>
<td>Collaboration agreement with Chiome Bioscience inc to evaluate LIV-2008b as an ADC of treat cancer</td>
</tr>
<tr>
<td>Preclinical study results</td>
<td>Mymetics (MYMX)</td>
<td>Mymetics’ HIV vaccine candidate confirmed promise in preclinical study with the Texas Biomedical Research Institute.</td>
</tr>
<tr>
<td>IPO</td>
<td>GeNeuro (GNRO)</td>
<td>GeNeuro was listed in Euronext raising about Euro 33 million through the admission to trading of 14,658,118 shares, including 2,538,500 new shares.</td>
</tr>
<tr>
<td>Study results</td>
<td>Ariad Pharmaceuticals</td>
<td>Ariad presented updated phase I/II clinical data on brigatinib in patients with ALK+ non-small cell lung cancer.</td>
</tr>
<tr>
<td>Grant</td>
<td>Basilea Pharmaceutica (BSLN)</td>
<td>Basilea awarded contract by BARDA of up to USD 100 million funding for ceftobiprole phase III program.</td>
</tr>
<tr>
<td>Milestone achievement</td>
<td>Kuros Biosciences (KURN)</td>
<td>Kuros received milestone payment of USD 1 million from Checkmate.</td>
</tr>
<tr>
<td>Research agreement</td>
<td>Saphetor</td>
<td>Saphetor signed collaboration with Lausanne University Hospital (CHUV).</td>
</tr>
</tbody>
</table>

**May 2016**

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Company/Partner</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>Product approval</td>
<td>Ferring Pharmaceuticals</td>
<td>Ferring announced approval for Nocdurna.</td>
</tr>
<tr>
<td>Financing</td>
<td>AC Immune</td>
<td>AC Immune raised USD 43.5 million (CHF 42.7 million) in financing round E.</td>
</tr>
<tr>
<td>Study results</td>
<td>Novigenix</td>
<td>Novigenix published multi-center study of Colox™ in clinical cancer research.</td>
</tr>
<tr>
<td>MAA validated</td>
<td>Actelion (ATLN)</td>
<td>The European Commission granted Actelion marketing authorization for Upravli (selexipag) in Pulmonary Arterial Hypertension.</td>
</tr>
<tr>
<td>Fast Track Designation</td>
<td>Santhera Pharmaceuticals (SANN)</td>
<td>Santhera received FDA Fast Track Designation for Omigapil for the treatment of Congenital Muscular Dystrophies (CMD).</td>
</tr>
<tr>
<td>Patent issued</td>
<td>Evolva (EVE)</td>
<td>Evolva was granted pivotal patent for commercial production of best-tasting fermentation-derived steviol glycosides.</td>
</tr>
<tr>
<td>Financing</td>
<td>Addex Therapeutics (ADXN)</td>
<td>Addex increased issued share capital and created treasury shares.</td>
</tr>
<tr>
<td>Study initiation</td>
<td>GeNeuro (GNRO)</td>
<td>GeNeuro announced first patients treated in Phase IIb study for Multiple Sclerosis.</td>
</tr>
</tbody>
</table>

**June 2016**

<table>
<thead>
<tr>
<th>Event Type</th>
<th>Company/Partner</th>
<th>Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>EMA PRIME program acceptance</td>
<td>Neurimmune</td>
<td>Neurimmune’s collaboration partner Biogen announced, that Aducanumab, its investigational treatment for early Alzheimer’s Disease (AD), was accepted into the European Medicines Agency’s (EMA) PRIority MEdicines (PRIME) program.</td>
</tr>
<tr>
<td>Study results</td>
<td>Santhera Pharmaceuticals (SANN)</td>
<td>New data from Santhera’s phase III trial (DELOS) in Duchenne Muscular Dystrophy (DMD) in neuromuscular disorders published.</td>
</tr>
<tr>
<td>Orphan Drug Designation</td>
<td>Debiopharm (TM)</td>
<td>FDA granted Orphan Drug Designation to Debiopharm’s IAP inhibitor Debio 1143 in the treatment of ovarian cancer.</td>
</tr>
<tr>
<td>Product approval</td>
<td>Evolva (EVE)</td>
<td>US FDA issued GRAS No Objection Letter for EverSweet™ next-generation sweetener.</td>
</tr>
<tr>
<td>License agreement</td>
<td>Selexis</td>
<td>Liomont signed commercial license agreement with Selexis for use of proprietary cell line and SURExEltron platform.</td>
</tr>
<tr>
<td>Study completion</td>
<td>Polyphor</td>
<td>Polyphor successfully completed clinical phase I study with POL6014 targeting life-threatening lung diseases including Cystic Fibrosis.</td>
</tr>
<tr>
<td>Refinancing</td>
<td>Therametrics (TMX)</td>
<td>THERAMetrics announced today an agreement to sell its Italian subsidiary THERAMetrics Clinical Supply Services.</td>
</tr>
<tr>
<td>Preclinical study results</td>
<td>Addex Therapeutics (ADXN)</td>
<td>Addex ADX71441 demonstrated positive results in non-human primate model of cocaine addiction.</td>
</tr>
<tr>
<td>Manufacturing agreement</td>
<td>Lonza (LONN)</td>
<td>Lonza and bluebird bio established a long-term commercial manufacturing agreement for Lenti-D™ and LentiGlobin™ drug products.</td>
</tr>
<tr>
<td>Refinancing</td>
<td>Therametrics (TMX)</td>
<td>THERAMetrics announced it had completed the sale of its CRO business to Accelovance.</td>
</tr>
<tr>
<td>Financing</td>
<td>GeNeuro (GNRO)</td>
<td>GeNeuro joined the CAC Mid &amp; Small, CAC Small and CAC All-Tradable Euronext indexes.</td>
</tr>
<tr>
<td>Study initiation</td>
<td>Cerbios</td>
<td>Clinical phase III to start during 2016 with the innovative dermatology spray delivery system AKYANO™.</td>
</tr>
<tr>
<td><strong>MAA validated</strong></td>
<td><strong>Santhera Pharmaceuticals (SANN)</strong></td>
<td>Santhera's Marketing Authorization Application for Raxone® in Duchenne Muscular Dystrophy (DMD) validated by the European Medicines Agency.</td>
</tr>
<tr>
<td><strong>License agreement</strong></td>
<td><strong>Selexis</strong></td>
<td>Progenics Pharmaceuticals signed commercial license agreement with Selexis.</td>
</tr>
<tr>
<td><strong>Financing</strong></td>
<td><strong>Kuros Biosciences (KURN)</strong></td>
<td>First trading day of new Kuros share after reverse split.</td>
</tr>
<tr>
<td><strong>Product launch</strong></td>
<td><strong>Basilea Pharmaceutica (BSLN)</strong></td>
<td>Basilea's antifungal CRESEMBA® (isavuconazole) launched in Italy.</td>
</tr>
<tr>
<td><strong>Acquisition</strong></td>
<td><strong>Finox</strong></td>
<td>BV Holding sold its equity stake in Finox to Hungarian Gedeon Richter.</td>
</tr>
<tr>
<td><strong>July 2016</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Award</strong></td>
<td><strong>T3 Pharmaceuticals</strong></td>
<td>University spin-off T3 Pharmaceuticals won Venture start-up award.</td>
</tr>
<tr>
<td><strong>Study initiation</strong></td>
<td><strong>Actelion (ATLN)</strong></td>
<td>Actelion initiated a phase III study to evaluate macitentan (Opsumit) in children with PAH.</td>
</tr>
<tr>
<td><strong>Study initiation</strong></td>
<td><strong>ObsEva</strong></td>
<td>ObsEva received clearance from US FDA to initiate phase IIb Study EDELWEISS with OBE2109, a potentially best-in-class oral GnRH antagonist, for the treatment of endometriosis.</td>
</tr>
<tr>
<td><strong>Study initiation</strong></td>
<td><strong>Actelion (ATLN)</strong></td>
<td>Actelion to enter phase II clinical development with new dual orexin receptor antagonist in patients with insomnia.</td>
</tr>
<tr>
<td><strong>Preclinical study results</strong></td>
<td><strong>Amazentis</strong></td>
<td>Milestone study on pomegranate anti-aging mechanism reported by Amazentis and EPFL researchers.</td>
</tr>
<tr>
<td><strong>Acquisition</strong></td>
<td><strong>Delenex Therapeutics</strong></td>
<td>Cell Medica announced the acquisition of Delenex Therapeutics, a privately held, clinical stage biopharmaceutical company focused on the development of locally and systematically applied antibody therapeutics.</td>
</tr>
<tr>
<td><strong>Filing</strong></td>
<td><strong>Santhera Pharmaceuticals (SANN)</strong></td>
<td>Santhera updated on US regulatory filing for Raxone® (idebenone) in Duchenne Muscular Dystrophy (DMD).</td>
</tr>
<tr>
<td><strong>Appointment</strong></td>
<td><strong>NeMoDevices</strong></td>
<td>NeMoDevices, a Swiss based developer in the innovative monitoring of brain blood flow and oxygen levels, announced the appointment of Dr. Philippe Dro as Chief Executive Officer of the company.</td>
</tr>
<tr>
<td><strong>Study initiation</strong></td>
<td><strong>Auris Medical</strong></td>
<td>Auris initiated ASSENT phase III trial of AM-111 for treatment of sudden deafness.</td>
</tr>
<tr>
<td><strong>Fast Track Designation</strong></td>
<td><strong>Auris Medical</strong></td>
<td>FDA granted Auris Fast Track Designation for Keyzilen™ (AM-101) in acute peripheral tinnitus.</td>
</tr>
<tr>
<td><strong>Financing</strong></td>
<td><strong>Relief Therapeutics</strong></td>
<td>Relief Therapeutics Holding announced the completion of the business combination with Relief Therapeutics and the conversion of a CHF 3.3 million convertible loan.</td>
</tr>
<tr>
<td><strong>Financing</strong></td>
<td><strong>Molecular Partners (MOLN)</strong></td>
<td>BVF Partners L.P., a US-based investor focused on biotechnology investments, acquired shares from pre-IPO venture capital shareholders.</td>
</tr>
<tr>
<td><strong>Collaboration agreement</strong></td>
<td><strong>Swiss Biotech Association</strong></td>
<td>Memorandum of Understanding between Korea Bio and Swiss Biotech Association signed.</td>
</tr>
<tr>
<td><strong>Financing</strong></td>
<td><strong>Auris Medical</strong></td>
<td>Auris secured loan facility of up to USD 20 million.</td>
</tr>
<tr>
<td><strong>Research grant</strong></td>
<td><strong>Evolva (EVE)</strong></td>
<td>Evolva’s nootkatone enters NIH-sponsored studies to assess its effectiveness against mosquitoes that transmit Zika virus.</td>
</tr>
<tr>
<td><strong>Service agreement</strong></td>
<td><strong>Selexis</strong></td>
<td>ASLAN Pharmaceuticals entered service agreement with Selexis SA for development of a proprietary cell line for expression of ASLAN004.</td>
</tr>
<tr>
<td><strong>Product launch</strong></td>
<td><strong>Evolva (EVE)</strong></td>
<td>Cornelius and Evolva bring new fermented resveratrol to market.</td>
</tr>
<tr>
<td><strong>Study initiation</strong></td>
<td><strong>ObsEva</strong></td>
<td>ObsEva initiated phase I clinical program of OBE022, a first-in-class orally active prostaglandin F2 antagonist, for the treatment of preterm labor.</td>
</tr>
<tr>
<td><strong>August 2016</strong></td>
<td><strong>Relief Therapeutics</strong></td>
<td>Relief Therapeutics announced signing of a term sheet to acquire FirstString Research.</td>
</tr>
<tr>
<td><strong>Collaboration agreement</strong></td>
<td><strong>Evolva (EVE)</strong></td>
<td>Collaboration with the US Navy to develop a new class of structural composite materials engineered from a polymer resin matrix fabricated from a specified formulation of Evolva’s resveratrol.</td>
</tr>
<tr>
<td><strong>Appointment</strong></td>
<td><strong>Kuros Biosciences (KURN)</strong></td>
<td>Kuros appointed Philippe Saudan as Chief Development Officer.</td>
</tr>
<tr>
<td><strong>Collaboration agreement</strong></td>
<td><strong>Polyphor</strong></td>
<td>Polyphor and Gilead established R&amp;D macrocycle drug discovery collaboration.</td>
</tr>
<tr>
<td><strong>Acquisition</strong></td>
<td><strong>Lonz (LONN)</strong></td>
<td>Lonza extended its reach in the healthcare continuum with acquisition of InterHealth Nutraceuticals.</td>
</tr>
<tr>
<td><strong>Product approval</strong></td>
<td><strong>Actelion (ATLN)</strong></td>
<td>Actelion received Swissmedic approval for Uptravi (sellexipag) for treatment of pulmonary arterial hypertension.</td>
</tr>
<tr>
<td><strong>Financing</strong></td>
<td><strong>ProteoMediX</strong></td>
<td>ProteoMediX, a diagnostic company developing non-invasive diagnostic tests for the accurate detection, prognosis and therapy selection of prostate cancer, announced the successful closing of an equity financing round.</td>
</tr>
<tr>
<td><strong>Marketing/Distribution agreement</strong></td>
<td><strong>Basilea Pharmaceutica (BSLN)</strong></td>
<td>Basilea announced distribution agreement with Hikma for CRESEMBA® (isavuconazole) in the MENA region.</td>
</tr>
</tbody>
</table>
Auris Medical announced top-line results from the phase III TACTT2 trial with Keyzilen® (AM-101) in acute inner ear tinnitus. The TACTT2 trial did not meet the two co-primary efficacy endpoints of statistically significant changes in tinnitus loudness and tinnitus burden compared to placebo.

Evolva (EVE) entered partnership on active pharmaceutical ingredients partner to fully fund development of new production routes for a family of APIs.

Actelion (ATLN) announced the completion of its first-line share purchase program. Actelion purchased 10,000,000 of its own shares, which represents 8.31% of the issued shares at the time of the start of the share purchases.

Relief Therapeutics announced that it has received the final cash settlement related to last month’s capital increase.

PaxVax inks Swiss marketing accord with Seqirus for flu vaccines.

Arbuths terminated license agreement for VLP platform for the treatment of hepatitis B infections.

Santhera received FDA grant in support of its ongoing phase I trial with Omigapil in Congenital Muscular Dystrophy.

Biogen's investigational Alzheimer's Disease treatment aducanumab granted FDA Fast Track Designation. Biogen is Neurimmune's collaboration partner.

Novimmune received milestone payment from collaboration with Genentech.

Auris Medical achieved midpoint for enrolment in phase III trial of AM-111 in sudden deafness.

Santhera's Idebenone (Raxone) received Orphan Drug Designation for Duchenne Muscular Dystrophy in Australia.

Selexis entered into commercial cell line license agreement with Pieris Pharmaceuticals for immuno-oncology bispecific drug candidate.

Santhera's Idebenone (Raxone) received Orphan Drug Designation for Duchenne Muscular Dystrophy in Australia.

Selexis Chairman and CEO Dr. Igor Fisch received prestigious award for Excellence in Leadership from BioProcess International.

Switzerland-based EngMab, a T-cell bispecific antibody developer, was acquired by Celgene for USD 600 million as part of an effort to pursue the development of treatments for multiple myeloma.

Molecular Partners regained rights to multi-DARPın® drug candidate targeting IL-13 & IL-17 for pulmonary indications from Janssen.

PX Therapeutics and Relief Therapeutics announced a strategic collaboration agreement for the recombinant production of atexakin alfa.

Selexis Chairman and CEO Dr. Igor Fisch received prestigious award for Excellence in Leadership from BioProcess International.

Molecular Partners presented data of MPD250 in an all-comer phase I study in solid tumor patients and updated on phase II studies.

Elanix, a developer of tissue regeneration products, announced the signing of supply agreements with two Swiss companies, Sincopharm and Tec-Pharma.

Appointment | EffRx Pharmaceuticals | Lorenzo Bosisio appointed CEO of EffRx Pharmaceuticals.
---|---|---
IPO | ADC Therapeutics | ADC Therapeutics raised USD 105 million in an oversubscribed round from existing investors.
Financing | CRISPR Therapeutics | CRISPR Therapeutics raised USD 91 million in US-listing and private placement.
Financing | Helsinn Healthcare | Helsinn Healthcare launched a new venture fund, Helsinn Investment Fund, with USD 50 million.
Financing | Lonza (LONN) | Lonza priced CHF 250 million five-year straight bond with a 0.125% coupon.
Patient enrolment | ObsEva | ObsEva randomized first patient in Phase Ib EDELWEISS study of OBE2109 for the treatment of endometriosis.
Collaboration agreement | Cerbios | Cerbios joined CMC Biologics and IDT Biologika in their strategic collaboration offering a fully integrated service for antibody drug conjugates.
Study results | Actelion (ATLN) | Scientific publications highlighted the unique profile of Actelion’s antimalarial compound.
Study initiation | Addex Therapeutics (ADXN) | Addex to conduct phase IIa proof of concept study of drupaglurant in focal cervical dystonia.
Capacity expansion | Biopôle | New building at Biopôle to welcome more life science organisations from 2018 on.
Rare Pediatric Disease Designation | Kuros Biosciences (KURN) | Kuros Biosciences’ KUR-112 receives Rare Pediatric Disease Designation.
Collaboration agreement | NBE Therapeutics | SOTIO and NBE Therapeutics signed collaboration and license agreement for next-generation antibody-drug conjugates.
Grant | MaxiVAX | Grant of CHF 240,000 awarded to Dr Nicolas Mach to evaluate the MaxiVAX cancer vaccine in patients with head & neck cancer.
Product Marketing | Evolva (EVE) | Evolva pre-launch portal for online product sales.
Study results | ObsEva | ObsEva announced results of the IMPLANT phase II trial of OBE001 (nolasiban) for the improvement of pregnancy and live birth rates following IVF/ICSI.
Collaboration agreement | Relief Therapeutics | Relief Therapeutics and FirstString Research announced a strategic collaboration for the development of atexakin alfa.
Collaboration agreement | Selexis | Selexis inks commercial cell line license agreement with ImmuNext, Inc. for anti-CD40L antibody being developed for treatment of chronic autoimmune disorders.
Study results | Debiopharm Group™ | Debiopharm reaches important development milestones for its staphylococcus-selective antibiotic Debio 1450.
Collaboration agreement | Debiopharm Group™ | Debiopharm announced clinical collaboration with the Merck-Pfizer Alliance in cancer immunotherapy.
Collaboration agreement | Evolva (EVE) | ERS Genomics and Evolva signed license agreement on CRISPR-Cas9 genome editing patents for industrial applications.
Financing | Inositec | Inositec secured CHF 1.4 million in seed financing to advance new class of inositol hexaphosphate-based drug candidates.
Manufacturing agreement | Lonza (LONN) | Lonza and Clovis Oncology signed strategic long-term manufacturing agreement to secure supply of rucaparib.
**November 2016**
License agreement | Actelion (ATLN) | Actelion obtained an option to in-license Vamorolone from ReveraGen.
Capacity expansion | Lonza (LONN) | Lonza opened its state-of-the-art pharmaceutical drug product services laboratories in the Stückli Science Park Basel (CH). Scientists in the new 1300 m² facility will focus initially on formulation development, drug product analytical development and quality control.
Collaboration agreement | Selexis | Selexis and Xencor entered strategic agreement, strengthening existing relationship for multi-specific antibody cell line development.
Study results | Actelion (ATLN) | Actelion announced positive results of the MERIT study with macitentan in patients with chronic thromboembolic pulmonary hypertension.
Marketing/Distribution agreement | APR Applied Pharma Research | Angelini and APR Applied Pharma Research strengthened their partnership in wound care with the launch of Nevodyn™ in the USA.
Appointment | Molecular Partners (MOLN) | Molecular Partners announced management change with Patrick Amstutz succeeding Christian Zahnd as CEO.
Marketing/Distribution agreement | Incyte Biosciences International | Incyte and GENESYS Pharma announced a commercialization agreement for Iclusig® (ponatinib) in Greece.
Product launch | Basilea Pharmaceutica (BSLN) | Basilea’s antifungal Cressemba® (isavuconazole) launched in France.
Collaboration agreement | Selexis | Selexis and OSE Immunotherapeutics collaborate to advance development of immunotherapies for cancer and autoimmune diseases.
<table>
<thead>
<tr>
<th>Appointment</th>
<th>AC Immune (ACIU)</th>
<th>AC Immune appointed experienced life science professional as new Chief Financial Officer.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Financing</td>
<td>T3 Pharmaceuticals</td>
<td>T3 Pharma closed first financing round to advance research and preclinical development of breakthrough bacteria-based cancer therapies</td>
</tr>
<tr>
<td>Acquisition</td>
<td>G7 Therapeutics</td>
<td>G7 Therapeutics, a spin-off from the University of Zurich has become a wholly owned Zurich-based subsidiary of Heptares and will be renamed Heptares Zurich.</td>
</tr>
</tbody>
</table>

**December 2016**

<table>
<thead>
<tr>
<th>IPO</th>
<th>Gour Medical (MLGML)</th>
<th>GOUR Medical, an animal health specialist, today announced the successful completion of its direct listing on Marché Libre Euronext Paris, the French securities market.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research agreement</td>
<td>Mymetics</td>
<td>Mymetics started research project with Sanofi for influenza vaccines.</td>
</tr>
<tr>
<td>Patient enrolment</td>
<td>Basilea Pharmaceutica (BSLN)</td>
<td>Basilea expanded oncology drug candidate BAL101553 clinical phase I/IIa oral study to include glioblastoma patients.</td>
</tr>
<tr>
<td>Orphan Drug Designation</td>
<td>PIQUR Therapeutics</td>
<td>PIQUR received Orphan Drug Designation from FDA for PQR309 in primary central nervous system lymphoma (PCNSL).</td>
</tr>
<tr>
<td>Patient enrolment</td>
<td>Auris Medical</td>
<td>Auris on track to resume enrolment of Keyzilen tinnitus program following regulatory feedback.</td>
</tr>
<tr>
<td>Study extension</td>
<td>GeNeuro (GNRO)</td>
<td>GeNeuro and Servier announced ANGEL-MS extension clinical study in multiple sclerosis.</td>
</tr>
<tr>
<td>Start-up</td>
<td>Neurimmune</td>
<td>Neurimmune and TVM Capital Life Science announced creation of AL-S Pharma to develop innovative therapy for patients with ALS.</td>
</tr>
<tr>
<td>Milestone achievement</td>
<td>Polyphor</td>
<td>Polyphor achieved milestone and extends R&amp;D collaboration with Novartis.</td>
</tr>
<tr>
<td>Study results</td>
<td>AC Immune (ACIU)</td>
<td>AC Immune partner Genentech presented important data on Alzheimer’s therapy Crenzumab.</td>
</tr>
<tr>
<td>Milestone achievement</td>
<td>Polyphor</td>
<td>Polyphor achieved milestone in Taisho collaboration.</td>
</tr>
<tr>
<td>Acquisition</td>
<td>Lonza (LONN)</td>
<td>Lonza acquired Capsugel to create leading integrated solutions provider to the global pharma and consumer healthcare industries.</td>
</tr>
<tr>
<td>Positive opinion</td>
<td>Actelion (ATLN)</td>
<td>Actelion received positive CHMP opinion for chloromethine gel (Ledaga) for the treatment of MF-CTCL.</td>
</tr>
<tr>
<td>Patent notice</td>
<td>Evolva (EVE)</td>
<td>Pivotal Evolva stevia sweetener patent received US notice of allowance.</td>
</tr>
<tr>
<td>Acquisition</td>
<td>Kuros Biosciences (KURN)</td>
<td>Kuros acquired Xpand in an all-share strategic transaction to create a leading commercial stage orthobiologics company.</td>
</tr>
<tr>
<td>Agreement</td>
<td>Actelion (ATLN)</td>
<td>Actelion and Johnson &amp; Johnson entered into exclusive discussions.</td>
</tr>
<tr>
<td>CE Filing</td>
<td>Kuros Biosciences (KURN)</td>
<td>Kuros submitted regulatory filing seeking CE certification for Neuroseal, a novel dural sealant.</td>
</tr>
<tr>
<td>Acquisition/IPO</td>
<td>Genkyotex</td>
<td>Genkyotex to merge with a French public biotech company Gentielc. Genkyotex’s shareholders will hold 80% of Gentielc’s share capital and voting rights. Exchange ratio is based on the actual value of Genkyotex established at EUR 120 million and of Gentielc established at EUR 30 million.</td>
</tr>
<tr>
<td>Promising Innovative Medicine Designation</td>
<td>Santhera Pharmaceuticals (SANN)</td>
<td>Santhera’s Raxone® designated Promising Innovative Medicine and suitable candidate for further evaluation under UK Early Access to Medicines Scheme (EAMS) for treatment in Duchenne muscular dystrophy.</td>
</tr>
<tr>
<td>Financing</td>
<td>InterAx Biotech</td>
<td>InterAx Biotech, a spin-off of ETH Zurich and Paul Scherrer Institute, closed a seed financing round with a team of Boston based biotech investors.</td>
</tr>
<tr>
<td>IPO filing</td>
<td>ObsEva</td>
<td>ObsEva, a clinical stage biotech developing therapies for women’s reproductive health and pregnancy, filed with the SEC to raise up to $86 million in an initial public offering.</td>
</tr>
</tbody>
</table>

Disclaimer:
This information was selected and compiled on the basis of publicly available information only. We therefore cannot guarantee that all events are included in the above summary for 2016.
Biotech continued its positive journey in 2016 although some of the key performance indicators did not reach the record heights of the previous years. Overall the US Food and Drug Administration approved 22 new drugs as compared with 45 in 2015 and 41 in 2014. The European Medicine Agency issued in total 81 positive opinions, slightly down on the 93 issued in 2015 and 82 in 2014.

In 2016, some 47 biotech companies launched an IPO in 2016 as compared with 78 in 2015. Of these, 24 US-based biotechs raised USD 1.2 billion as compared with 2015, when 45 companies raised USD 3.8 billion. Some 23 European companies achieved a total of USD 0.7 billion compared to 33 raising USD 1.4 billion in 2015.

The total amount of capital raised via IPO in 2016 was about half of the amount raised in 2015. This was a clear reflection of uncertainty created by the presidential elections in the US as well as the unknown outcome of BREXIT and its implications for the European biotech universe.

Swiss biotech landscape

These global trends were also reflected in the Swiss biotech landscape. The Swiss biotech industry achieved total revenue of CHF 5.7 billion (2015: CHF 5.1 billion). This result is very positive, especially as the number of revenue-generating biotech companies has increased over the past years. It is also a sign of a certain maturity in the Swiss biotech industry as some of the products are well received in the market and the corresponding demand continues to increase. However, more revenue does not automatically translate into better profitability. A larger proportion of the biotech companies are still in a loss-making position and only a few of the more established companies are generating stable profits.

Key developments in product approvals and clinical development include Actelion’s sellexipag. This was approved by Health Canada and the Committee for Medicinal Products for Human Use (CHMP) in January 2016 as well as Swissmedic in summer 2016. Basilea’s isavuconazol (Cressembal®) was also approved by various European countries.

A series of positive study results were communicated by companies such as AC Immune, Addex, GeNeuro, MaxiVax, Neurimmune, Novimmune and Polyphor. Some of those study results triggered double-digit milestone payments for the Swiss biotech companies from their collaboration partners. Other companies – e.g. Auris Medical with its AM-101 phase III trial – had to digest some setbacks.

Positive momentum in financing

The Swiss biotech community was able to raise almost CHF 823 million (2015: CHF 907 million). Public companies raised approximately CHF 351 million (2015: CHF 474 million) and private companies harvested CHF 472 million in private rounds (2015: CHF 433 million). ADC Therapeutics located in Epalinges was able to achieve one of the largest private rounds in Europe with the collection of USD 105 million. Cardiorentis and Novimmune also cashed in each with CHF 60 million rounds.

In 2016, three Swiss biotech companies successfully completed an IPO. However, all of these IPOs took place abroad; two on NASDAQ (AC Immune, CRISPR Therapeutics) and one at Euronext in Paris (GeNeuro). AC Immune was the most successful IPO of a European biotech company in 2016. These three IPOs combined collected more than CHF 200 million in gross proceeds by going public. In December 2016, another two biotechs announced their intention to do a listing at a foreign exchange. ObsEva’s IPO on NASDAQ was successfully completed in January 2017, and Genkyotex’s reverse merger with the French company Gentici resulted in another Euronext listing.

SIX Swiss Exchange reported two reverse mergers. During the 1st quarter of 2016 Cytos was completely absorbed by Kuros BioSciences (thereby becoming a medtech company). During the summer months, Relief Therapeutics completed another reverse merger with Therametrics Holding, which was itself the result of a reverse merger back in 2013 (Mondobiotech).

Also worth noting is the fact that Lugano-based Helsinn launched its own venture fund with an initial capital injection of USD 50 million.

M&A and collaborations

Big and specialty pharma’s need for new growth opportunities has been discussed in depth in the EY Firepower Index and Gap Report in early 2016. Some of the impacts on the Swiss biotech landscape are outlined in more detail below.

Delenex Therapeutics, a spinoff from Esbatech, was acquired in summer of 2016 by CellMedica UK. Finox was sold by BV Holding to the Hungarian company Gedeon Richter. This was the 2nd acquisition in Switzerland after Preglem back in 2010. EngMab, located in Schwyz, attracted Celgene to acquire the company for a total of USD 600 million. The University Zurich spinoff G7 Therapeu-
On 26 January 2017, the US life sciences giant Johnson & Johnson announced its decision to acquire the European biotech star Actelion in an all-cash acquisition with a deal value of USD 30 billion. This transaction will include the planned spin-off of the Actelion R&D unit in a new and independent, SIX-listed company called Idorsia. Being a 2017 deal, this transaction will be included in the 2017 deal statistics and charts of the Swiss Biotech Report issued in 2018.

Also on the collaboration front, various Swiss companies were able to attract well known partners. Here are a few of the deals:

- Piqur Therapeutics with Eisai
- ADC Therapeutics with Chioke BioSciences
- Sophia Genetics with Illumina
- Selexis with Xencor
- GeNeuro with Servier

Overall, 2016 was again a very positive year for the Swiss biotech industry. The industry achieved a lot of progress in many development fields and the positive news flow is a confirmation of the maturity of the sector as a whole. Swiss biotechs are continuing to attract financial as well as industrial investors which is needed for a prosperous industry.
Facts & figures

Number of biotech companies in Switzerland

Number of employees

Notes

– The 2016 data in this table is based on information that was available up until March 2017 when this report was compiled. At this time, some of the companies had not yet disclosed their final financial figures for 2016. Therefore, some figures were carefully extrapolated on the basis of the latest interim data publicly available (e.g. Q3 2016).

– Selected financial figures for biotech activities of Lonza’s business segment “Pharma & Biotech Market Segment”, which has been established as part of the reorganization at Lonza, are included for 2016. For the previous periods presented, Lonza’s “Bioscience” and “Biological Manufacturing” are included based on actual figures publicly available or careful estimates. Lonza’s “Pharma & Biotech Market Segment” respectively “Bioscience and Biological Manufacturing business sectors” are presented due to Lonza’s transformation into a life sciences company and its inclusion into the ICB Biotech Sector and the SXI LIFE SCIENCES® and SXI Bio+Medtech® indices at the SIX Swiss Exchange.
As some privately held companies do not disclose financial figures, the figures above represent EY’s best estimate.

All figures are headquarters-counted and do not include data from pharma companies such as Novartis and Roche.
Publicly traded Swiss biotech companies

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<tr>
<th>Year</th>
<th>Revenues (CHF million)</th>
<th>R&amp;D expenses (CHF million)</th>
<th>Profits/losses (CHF million)</th>
<th>Liquidity (CHF million)</th>
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<td>2016</td>
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<td>906</td>
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<td>1403</td>
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Source: Annual Reports, website information and EY

Privately held Swiss biotech companies

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<th>Year</th>
<th>Revenues (CHF million)</th>
<th>R&amp;D expenses (CHF million)</th>
<th>Profits/losses (CHF million)</th>
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<tr>
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<td>771</td>
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<td>898</td>
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</tbody>
</table>

Source: EY
Impressum

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