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European Biotechnology

Life Sciences and Industry Magazine

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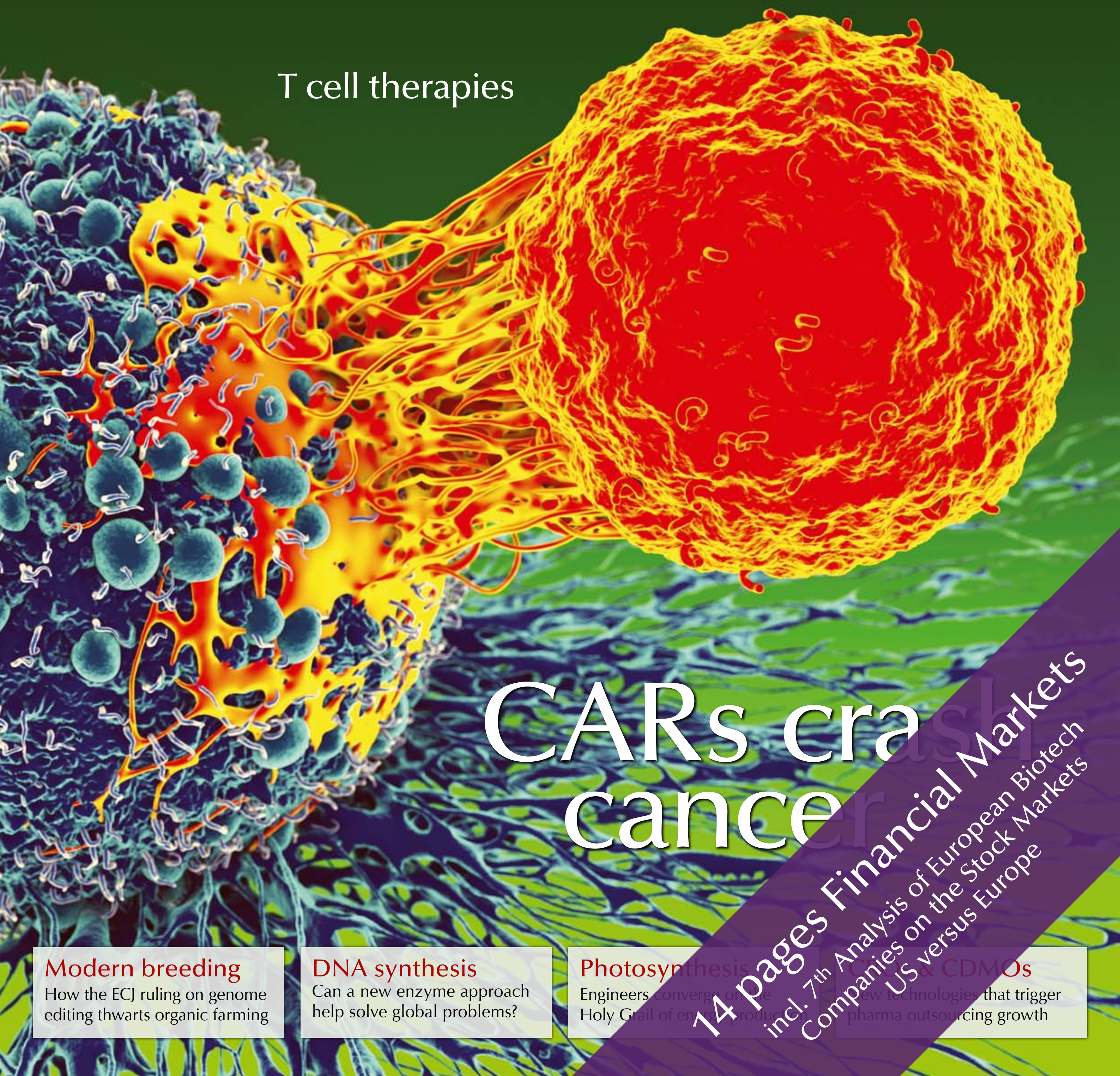
Interview

Novozymes's New Business Development Head Sebastian Søderberg on the value of open innovation.



T cell therapies

CARs crash cancer

14 pages Financial Markets

incl. 7th Analysis of European Biotech Companies on the Stock Markets US versus Europe

Modern breeding
How the ECJ ruling on genome editing thwarts organic farming

DNA synthesis
Can a new enzyme approach help solve global problems?

Photosynthesis
Engineers converge on the Holy Grail of energy production

CMOs & CDMOs
New technologies that trigger pharma outsourcing growth

Sustained optimism

REPORT

ANALYSIS OF EUROPEAN BIOTECH COMPANIES ON THE STOCK MARKET

Biotech stock markets are still appreciated by investors. Whereas the number of IPOs significantly decreased in the first half year of 2018 compared to 2017, follow-on financings doubled. This is particularly true for European stock exchanges. Nurtured by the further progress of breakthrough technologies such as CAR-T for cancer therapies, listed European biotech companies profit from a sustained optimism among investors.

Biotech stockmarkets have developed reasonably well in 2018 so far and IPOs are still a viable route to access further capital. Although there have been no record-breaking highs, an overall growth trend is still obvious. According to the analysis, which also includes all European biotech firms listed on the US Nasdaq, all of the key figures for 2018 so far show a sustained optimism. The 240 European biotech companies raised a total of €2.54bn in financial proceeds by the half year of 2018 – 40% more than in the same period of time in 2017 (€1.81bn) (see Fig. 1). When it comes to IPOs and listings, however, 2018 showed a lower activity. A total of five European biotech IPOs took place, raising a total figure of €355m. This means a slight increase of 4% compared to the same period in 2017 (see Fig. 2). Four companies opted for one of the 14 European trading centres, and one floated on US Nasdaq.

€355m

Amount of money raised via IPOs by European biotech companies in HY 2018.

Five IPOs in 2018

Whereas Swiss company Polyphor SA raised a very high volume of €130m and also Swedish Calliditas Therapeutics AB could raised €72m, the other Europe-based IPOs rested more at the lower end – Polish OncoArendi Therapeutics S.A. (€13.7m), Danish ViroGates A/S (€10m),. The Nasdaq IPO of UK-based Autolus Therapeutics reached a total of €129.5m. In addition to the IPOs, two new listings that did not raise additional money took place on the Nasdaq Nordic Stock Exchange in Stockholm (Fluicell AB and Gabather AB). With this activity, the list of the most attractive stock market locations changed slightly. Paris (47) is still at the top, although it has had no biotech IPOs so far in 2018. Currently, Stockholm (44) and London (44) share second place; the stock exchange in Sweden is now home to three more listed biotech companies. The shares of 39 European companies are currently traded on US Nasdaq. In addition to the IPO, two secondary listings (MorphoSys AG and Biofrontera AG) took place.

Picture: peshkov/istockphoto.com

Follow-on financings

In 2018, investors spent even more money on European biotech companies compared to the same period in 2017. In the first half of this year, a total of €2.18bn was dropped into these companies via follow-on financings, a substantial increase of 48% compared to the same period in 2017 (see Fig. 3). The average size of capital increase in 2018 was a bit higher (€28m) compared to €25m in the same period in 2017. Within Europe, Euronext and Alternext together demonstrated the most activity, with 19 financings and total proceeds of €321m, followed by AIM in London (13 financings, €93m) and Frankfurt (11 financings, €88m). The US-listed companies brought in a total of €1.21m capital, with 14 financings, a 50% increase compared to half year numbers of 2017.

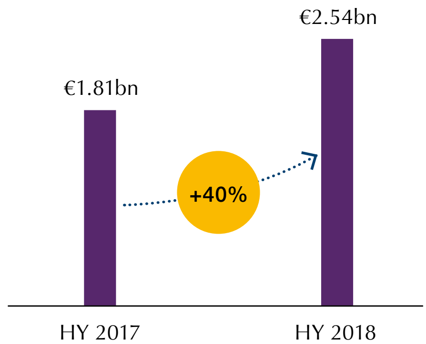


Fig. 1: Total financial proceeds of European biotech companies

Oncology in the spotlight

The vast majority of companies (85%) are active in the health sector, developing diagnostics or new therapies for which major investments and long-term financial strategies are required. All of the five stock market newcomers in 2018 can be assigned to this category. The most attractive field within the health area is oncology (see Fig. 4). A total of 74 com-

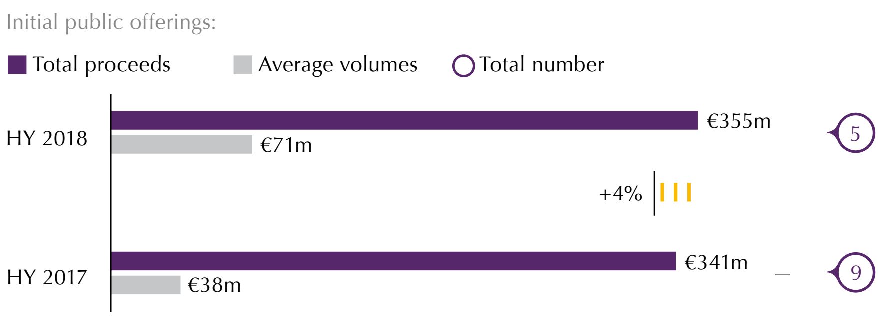


Fig. 2: Number of IPOs and capital raised

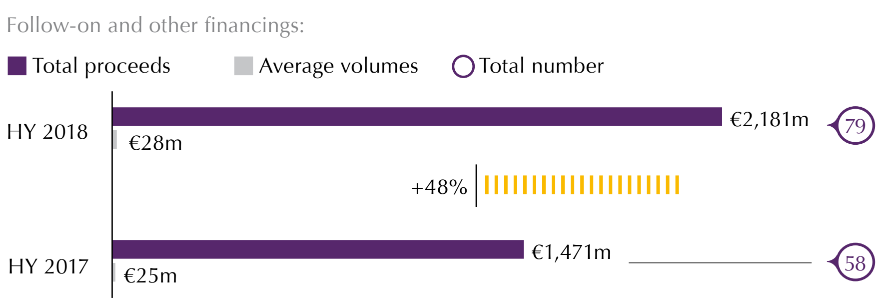


Fig. 3: Number of financing rounds and capital raised

REPORT

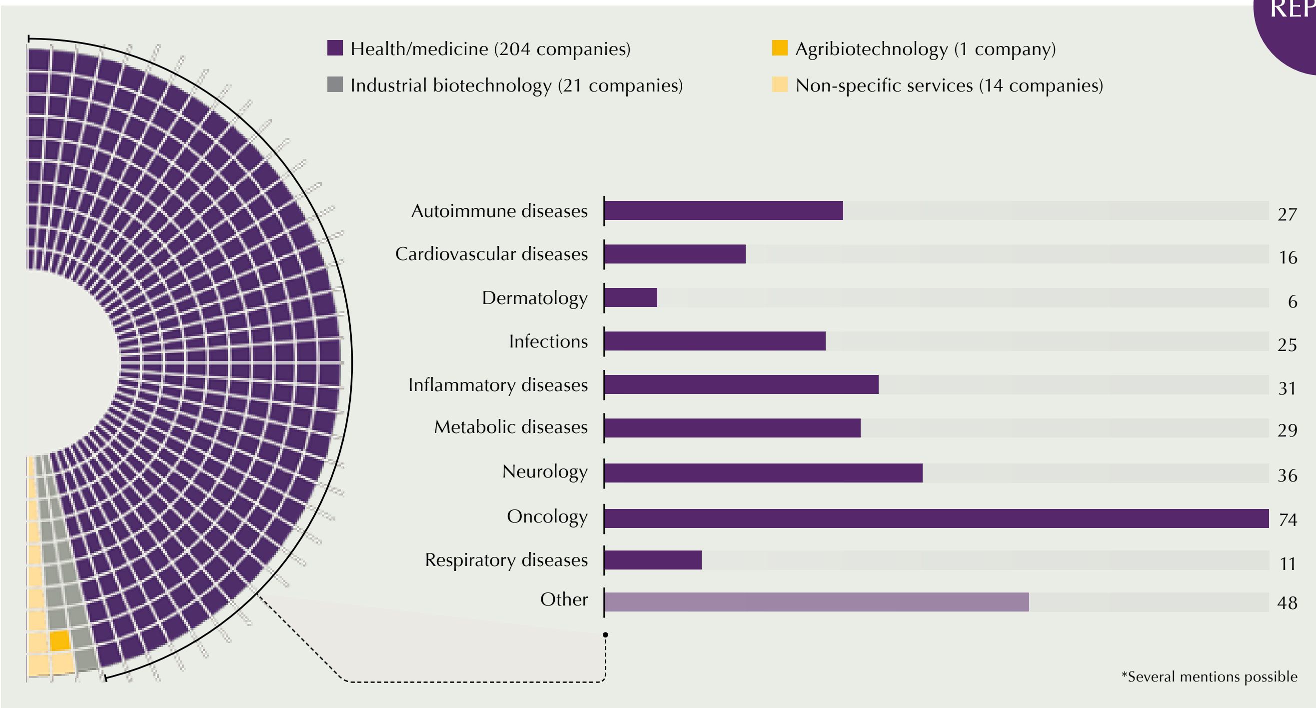


Fig. 4: Fields of activity and the areas of indications* medical biotech companies address

panies operate in this field, followed by neurology (36), inflammatory (31) and metabolic diseases (29), as well as autoimmune diseases (27).

Service providers that offer biotech-based processes for others in the B2B environment have a completely different risk profile than companies focused on biopharma. Although mid- and large-cap companies such as bioMérieux and Eurofins fall into this category, only 14 companies overall operate in this field. Another area of listed European companies is industrial biotechnology. A total of 21 firms are involved in the development of new enzyme-based processes or biobased solutions for various industries. With 14 different trading centres, the variety of stock exchanges relevant to European biotech companies is huge. Analysis of previous years has revealed that the cross-border stock market Euronext is especially attractive for European biotech companies, as it clearly provides a critical mass of listed biotech companies as well as a nurturing environment in terms of innovation and high-risk financing. However, in 2018, less activity took place here and no biotech company went public. But the Euronext-listed companies succeeded with follow-on financings – in particular those with a double listing in the US (Cellectis and DBV Technologies). The first half-year of 2018 also demonstrated that the other cross-over exchange in Europe, the Nasdaq Nordic, is catching up. With the IPO of ViroGates A/S in Copenhagen, two new listings at Stockholm First North, and three Swedish companies changing from First North in Stockholm to Nasdaq Nordic Main (Nuevolution A/S, Immunovia AB, Immunicum AB), significant activity took place there in 2018.

Another sign for sustained optimism in the European stock market comes from the two well-received IPOs in Switzerland and Poland. That the antibiotics developer Polyphor succeeded in raising €130m in its stockmarket debut on the Swiss Stock Exchange (SIX) demonstrated the high potential of life sciences capital available for attractive biotech stories, even in challenging markets such as anti-infectives. At the same time, it underlined the strong position of SIX in 2018. Reproductive health specialist ObsEva, already listed on Nasdaq, also announced a new listing in Switzerland.* The IPO of Polish drug developer OncoArendi on WSE increased the

Key facts of the European public biotech sector

- 240 public European biotech companies*
- 39 European biotech companies listed on US Nasdaq
- 5 IPOs with €355m capital raised in HY 2018 (+4%)
- 79 financings with €2.2bn capital raised in HY 2018 (+48%)
- Total financial proceeds of €2.54bn in 2018 (+40%)

REPORT

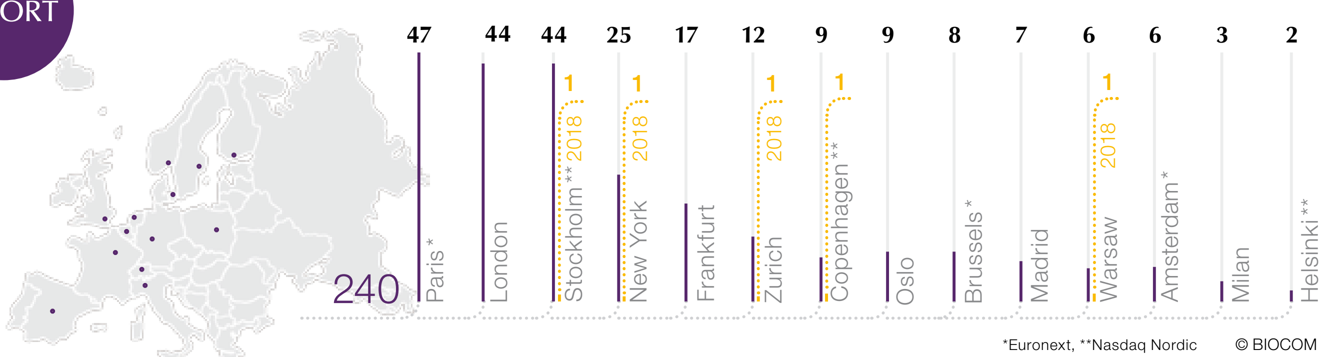


Fig. 5: Overview of trading centres with total numbers of listed European biotech companies and IPOs in 2018

number of listed companies in Warsaw to seven. The company, founded in 2012, focuses on novel therapeutics for neoplastic and inflammatory diseases. They have an asthma-treatment candidate in clinical Phase 1 and an immunotherapeutic approach – based on arginase inhibitors to be used as a combination therapy for the treatment of patients with colon, lung, skin, or brain cancer – in preclinical development. The IPO was met with significant demand from both institutional and individual investors and the proceeds are aimed at bringing forward licensing agreements and strategic partnerships on an international level.

€2.54bn

capital raised by European biotech companies on the stock markets in HY 2018.

Fewer new entries on Nasdaq

The first six months of 2018 saw quite modest activity for new European biotech companies on Nasdaq. The only IPO took place in June, when cancer biotech Autolus Therapeutics plc from UK went public in New York. The company, which is developing blood cancer therapies based on highly targeted CAR T cells, succeeded in raising a total of €129.5m, with a share price at the upper end of the range. In addition, two already-listed German companies decided to go for a secondary listing on Nasdaq this year: MorphoSys AG (€168m) and Biofrontera AG (€10m). Antibody specialist MorphoSys gained much interest due to its late-stage biotech drug candidate MOR208, for which market approval is within reach.

So far, overall activity for 2018 demonstrates a positive stock market development for European biotech companies. But traditionally, the first half year shows lower activity than the second half of the year. For this reason, many experts expect an ongoing positive trend, so that numbers in the upcoming month may possibly exceed those recorded in the first six months.

* Please note: Secondary listing took place 13/07/18 and is not included in half-year-data of 2018 for this report.

Report is available online:
www.biocom.de/en/analysis2018

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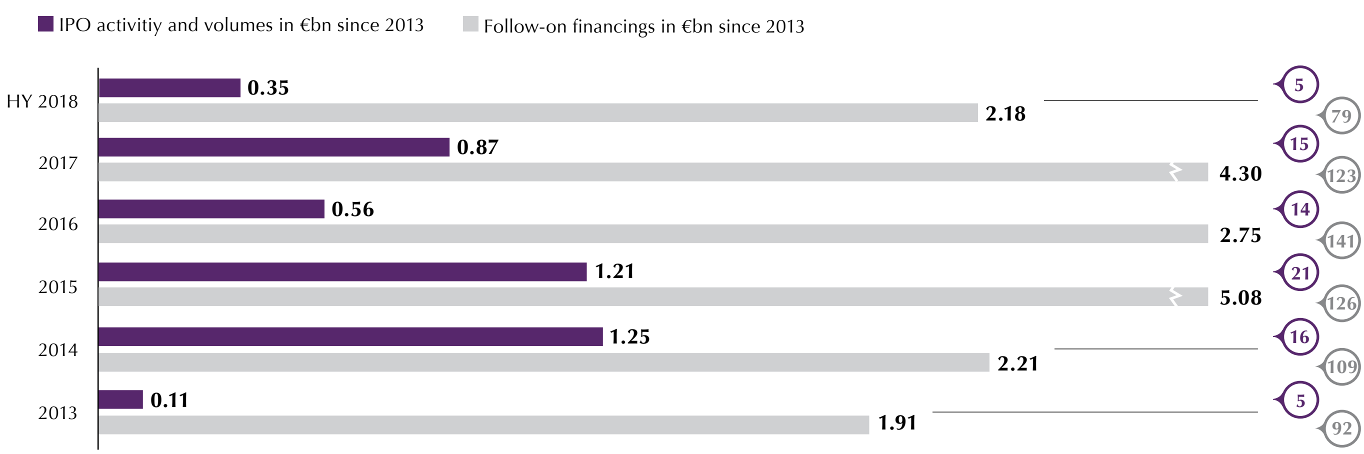

Overview of IPO activity and follow-on financings of European listed biotech companies since 2013

Promising company stories attractive for US investors

REPORT

EUROPEAN BIOTECH COMPANIES ON NASDAQ Due to its broad spectrum of investors, the US Nasdaq continues to be an attractive stock market for European biotech companies, particularly when they are in late-stage development or active in promising areas such as immunotherapies. In 2018, Nasdaq saw one European biotech IPO, two secondary listings from European companies, and strong follow-on financings. Overall figures are much higher compared to 2017.

Key facts of European listed biotech companies: US vs Europe

	Nasdaq US	US/Europe	Europe	Total numbers
Number of European biotech companies	25	14	201	240
Capital raised via IPOs/listings in HY 2018	€ 129.5m	€ 178.4m	€ 225.8m	€533.7m
Capital raised via follow-on financings in HY 2018	€ 578.4m	€ 458.3m	€966m	€2.0bn
Total proceeds in HY 2018	€ 707.9m	€636.7m	€1.13bn	€2.54bn

IPOs and listings on Nasdaq are particularly interesting for companies which need a large amount of capital. This holds true for the field of CAR-T-focused companies at the beginning stage of clinical development, such as Autolus Therapeutics. The company was spun out from University of London in 2014, has a pipeline of product candidates in development for the treatment of haematological malignancies and solid tumors, and in June 2018 achieved a successful IPO on Nasdaq, raising €129.5m in total at the upper share price range.

Unbroken investors' appetite

Compared to last year, the volume increased by 44%. The only IPO in the first half of 2017 was Swiss ObsEva, which brought in €90m. However, IPO volumes in 2018 were rather atypical: the largest volumes in the US and Europe were nearly at the same level – both approximately €130m (Polyphor and Autolus). In total, 39 European biotech companies were listed on Nasdaq at the end of the first half of 2018. They raised total financial proceeds of about €1.3bn via IPOs, secondary listings, and follow-on financings. This is a significant gain of 50% compared to the same period in 2017 (€897.5m), demonstrating an unbroken investors' appetite in European biotech companies. For the second year in a row, capital investments show a growth trend not only in numbers, but also in volumes. The development is driven by a constant flow of good company news, primarily from technology firms focusing on new therapeutic approaches such as gene therapy, CRISPR or cancer immunotherapies. Other more uncertain conditions – such as the US president's pharma strategy – apparently had less influence on the stock market. Experts foresee an ongoing positive trend for biotech companies on US Nasdaq in 2018.

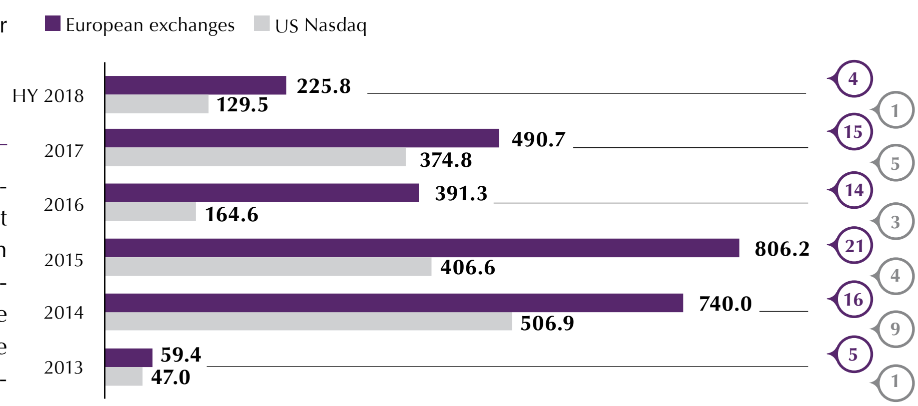

Fig. 1: Comparison of IPO numbers and volumes (in €m) raised by European companies

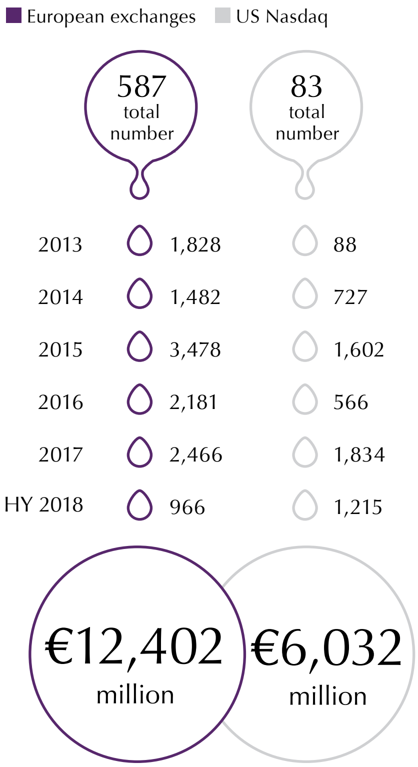

Fig. 2: Overview of follow-on financings in €m since 2013

50% increase in total financial proceeds

The 39 listed European biotech companies attracted a combined total of €1.215bn in 14 follow-on financings, which means an increase of 50% compared to 2017 at the same time (€807.5m; 9 financings). The numbers also include the two secondary listings of German biotech companies MorphoSys and Biofrontera, which amounted to a total combined capital of €178.4m.

Compared to their counterparts that are only listed on European stock exchanges, the firms on the US Nasdaq not only generated more capital in total numbers, but also with much greater average volumes (US: €86.8m vs. Europe: €14.9m). This again demonstrates that US Nasdaq offers a valuable platform for clinical stage companies with a high capital demand. ■

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"Open window will hold on"

VC CAPITAL PERSPECTIVE For private investors, Nasdaq rather than Europe is often the preferred place for a biotech IPO, says Karl Nägler, Partner Health & Care at European investment firm Gimv.

Karl Nägler, Partner, Health & Care, Germany, joined Gimv in 2011. Previously, he worked at Ventech in Paris and Atlas Venture in London and Munich. Nägler holds a PhD in molecular biology.

EuroBiotech_ Do you think at present it's a good time for a biotech company to go public?

Karl Nägler_*Already for some years now, we see an open IPO window for biotech. This is particularly true for US Nasdaq for which we saw very good performing numbers during the recent months and promising companies active in e.g. gene therapy, or immunotherapeutics who have had positive news flow. This development also has an influence on the European stock markets: if Nasdaq Biotech indices are going up, Europe is also well performing. At present, no dramatic downswing is visible in the US, although from my perspective current indices already tend to reach record levels from 2015. The open window seems to hold on.*

EuroBiotech_ How do you evaluate Europe as a stock market location?

Karl Nägler_*Whilst observing the European stock market during the recent years, we have seen a quite positive development. At Euronext in particular, a substantial number of biotech IPOs took place, but since 2018 this development decelerated a bit – due to some negative news flow in 2017 about listed companies e.g. at Euronext Paris. For this reason, I think, at the time being, more mature biotech businesses are requested by investors in Europe. In addition, we see less specialist investors active in Europe. Generalists usually look for safer investments and business models they can understand and are often not interested in early stage companies. This means: if you are planning a stock market debut, your company story should fit into their scheme, otherwise it will be difficult to hold performance levels high in the long-term.*

EuroBiotech_ So you would advise biotech companies to have a look at Nasdaq?

Karl Nägler_*We at Gimv always evaluate an IPO very openly, both in the US and in Europe. The decision really depends on the development stage of the respective company, its business model, investor base and origin, its liaison with the US market. What speaks for Nasdaq: the liquidity is much higher and you will easier find comparable companies with similar business models. This makes it easier to receive an adequate market capitalisation.*

EuroBiotech_ So far, IPO activity for European companies was very modest. Do you see any reasons for that?

Karl Nägler_*I think there is no empty pipeline and I expect to see more activity soon. You have to take into account that candidate companies need to be at the right stage of development. Furthermore, it takes time to prepare them for such a step – in particular, if the IPO is planned in the US. You have to make sure that the firm is known by US investors and that the management team is ready for this transatlantic task.* ■

Picture: Gimv

Retrospective: Biotech Listings on the Swiss Exchange

REPORT

BY CHRISTIAN FEHR An IPO is a veritable option for funding biotech companies. This has been proven by the successful listing of a number of companies on SIX in the past two decades.

The success of Lonza going public in 1999 paved the way for the Actelion listing on SIX in the following year. Actelion pioneered biotech company listings and it became the largest European pure-play listed biotech firm over time. In 2016, the Actelion success story culminated in a US$30 billion takeover bid by Johnson & Johnson.

Today, SIX is one of the leading biotech exchanges in Europe and it hosts the highest capitalized European biotech company. Things started to take off following the Cytos (now Kuros Biosciences) IPO in 2002. In the period 2004 to 2007, SIX welcomed four new biotech companies: Basilea, Santhera, Newron and Addex. And it was also around this time that the SXI Bio+Medtech Index was created, underpinning the strong commitment of SIX to the biotech sector.

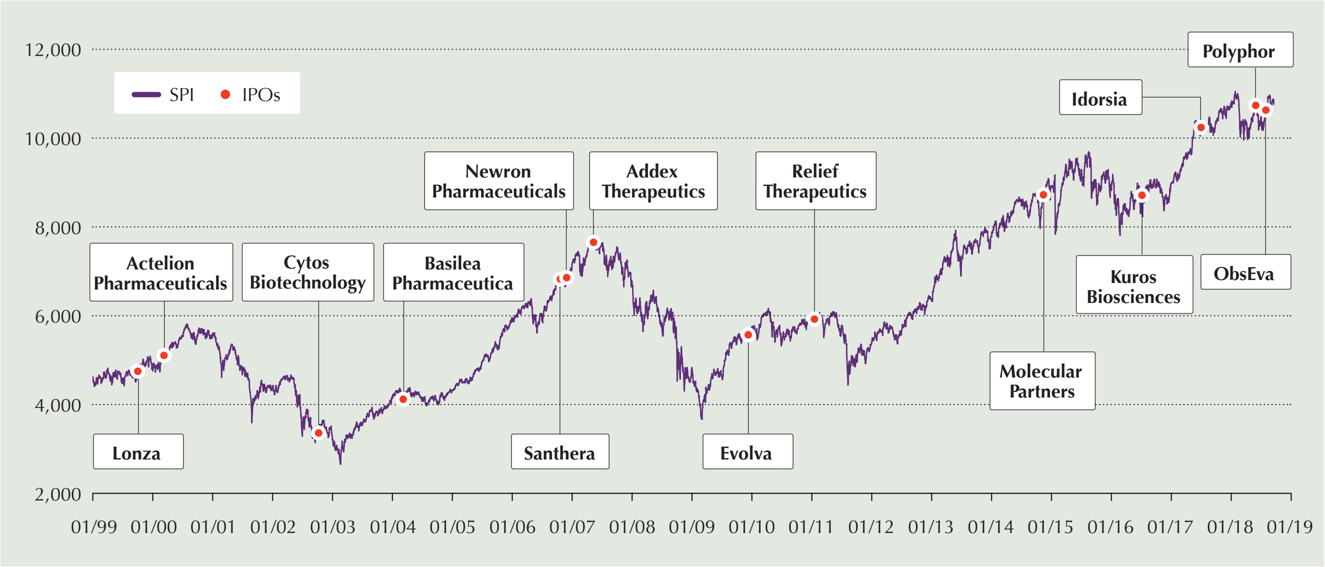
After the listing of Evolva and Mondobiotech (now Relief Therapeutics) in 2009, there was something of a break in biotech listings and then Molecular Partners in 2015 heralded a new era. In 2017, Idorsia, the company spun off as a contribution-in-kind to the former shareholders of Actelion, was listed and achieved a market capitalization of around CHF 1.5 billion on the first trading day.

Christian Fehr
Relationship Manager Primary Markets, SIX

“It’s very important for Idorsia to be quoted on the same stock exchange as big companies such as Novartis, Roche but also Lonza, many suppliers and many companies involved in biotech.”

Jean-Paul Clozel, CEO Idorsia

In the current year 2018, SIX welcomed with Polyphor and ObsEva (dual primary listing) two more pure-play biotech companies. The listing of Polyphor allowed the company to raise CHF 155 million and was one of the largest European biotech



Biotech listings on the Swiss Exchange in the past two decades

Picture: SIX, Source: SIX

	Light	Standard	Premium	Deluxe
Informatoin, Education & Network by SIX	✓	✓	✓	✓
Factsheet by Morningstar	✓	✓	✓	✓
Research Coverage by Baader Helvea, Bank Vontobel, Zürcher Kantonalbank		✓ by one bank	✓ by two banks	✓ by three banks

Source: SIX

IPOs in recent years, in terms of proceeds raised by an issuer to finance the development of its pipeline. Obseva, already listed in the US, chose to list on SIX for various reasons including to raise its profile among Swiss and European investors and provide another robust market for any future potential financing activities. This impressively underlines the continuing attractiveness of the Swiss exchange for life sciences and in particular biotech companies – regardless of size.

In summary, 14 biotech companies listed on SIX in the past two decades and they aggregated a market capitalisation of around CHF 30 billion as per mid-August 2018. There have been other impressive examples of listed companies in the space, which are not counted in this number. For instance Cosmo, which over time developed from its biotech origins into more of a pharmaceutical company.

The prominent global pharmaceutical players Novartis and Roche feature in the issuer base of SIX and they lay the foundation for a well-diversified peer group whose strong appeal reaches far beyond Switzerland's borders. It therefore comes as no surprise that SIX ranks as Europe's most important life science exchange and leading biotech listing location. Switzerland's capital-rich investor base, powerful banking system and its industry expertise make up the country's dynamic life sciences ecosystem. This allows companies to efficiently raise capital with a view to driving scientific discovery through to market launch. The Lonza experience (see quote) is proof of this. Between January 2017 and August 2018, SIX-listed biotech companies raised about CHF 3.5 billion equity capital.

How SIX supports listed biotech companies

Achieving trading liquidity and adequate analyst coverage has become more challenging given the increase in regulations. As a result, listed biotech companies need to recognise that these are important issues and address them accordingly. Alongside other initiatives, the SIX Stage Program provides the means for doing so.

"Successful IPOs and capital raisings in 2017 and 2018 confirm the deep pools of capital available in Switzerland. For example, Lonza raised over CHF 3.1 billion in two capital increases which marked the largest equity funding by a SIX listed non-financial corporate last year."

Thomas Zeeb,
Head Securities & Exchanges, SIX

One of the most important reasons for listing on an exchange is the facilitated access it gives to the capital market and therefore to growth capital. However, to use capital markets effectively, a company needs to have a minimum volume of trading liquidity. Shares of small and medium-sized companies are often less liquid for a variety of reasons.

SIX offers several services and initiatives such as the Stage Program to support companies in the process of building their presence in the market and achieving an appropriate valuation. Companies benefit from a regularly updated factsheet and research reports prepared by experienced partners and can thus reach a larger number of capital market participants.

"We were the first company to join the Stage Program in 2016 and have noted increased investor awareness and interest due to the additional analyst coverage, since."

Stefan Weber, CEO Newron

Through SIX, companies also gain access to statistics and services that facilitate the "Being Public". To guarantee the independence of the reports and strengthen the trust of investors in the research, no contractual relationship exists between the listed company and the research provider. SIX acts as a link between the two. In addition, a research committee has been set up to ensure the interests of the different parties are taken into account. It is an advisory body to SIX.

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Coming of Age

VENTURE CAPITAL A quick walk through the last 20 years of biotech investing in Europe and a snapshot of the state of the industry today. A new mode of action has been established and the key ingredients for successfully financing innovative therapies and treatments for the benefit of patients in today's globalised market environment have been defined.

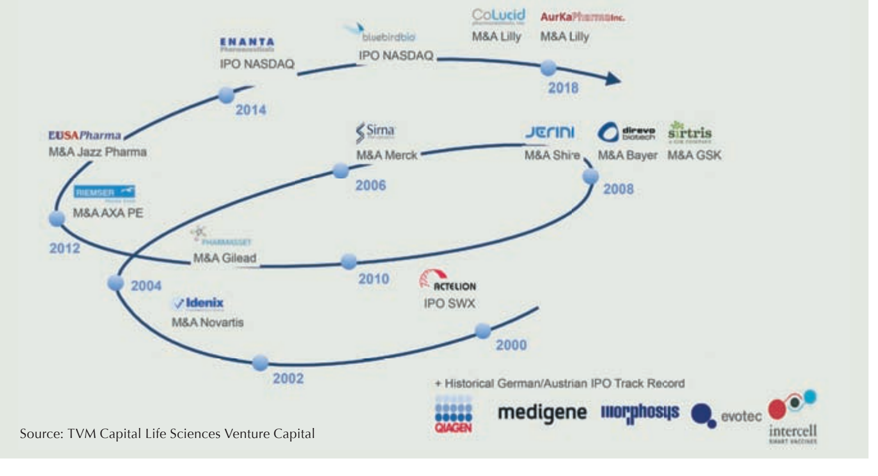
› Dr. Hubert Birner, Managing Partner, TVM Capital Life Science

The biotech industry in Germany and Europe can now claim a history of more than two decades. Looking back at the life cycle of this industry, we can certainly identify some shifts and milestones that triggered major change.

In the early days of investment in biotechnology and life sciences – at least in Germany – federal programmes were set up to support acadaemia with promising biotech projects. To facilitate the development of an 'entrepreneurial spirit' within these circles, the role of investors, especially venture capital investors, focused on building well-functioning companies around the idea of an entrepreneur. The necessary capital and network of expertise was provided, and syndicates of investors financed within several rounds to finally IPO the company at one of the relevant stock exchanges. The IPO usually was a form of exit and financed the commercialization of at least one product candidate. Risk mitigation was handled on company level; they were to build a broad, multi-stage product pipeline that ensured the development and growth on a long-term scale.

Venture capitalists had to get disruptive

The year 2008 was a memorable year for the global economy at large and inevitably for the biotech industry and all players in the industry – namely venture capital providers. However, the meltdown of the financial markets in late 2008, although it had its well-known implications on all of us, was not the start of a phase of rethinking the finance model in the industry. That started even earlier. The "pharmaceutical ecosystem" was already transforming. Emerging markets were gaining significance, while the established pharmaceutical markets of Western Europe and the U.S. grew more slowly. The pharmaceutical business underwent major reconstruction and demanded higher capital efficiency. Undoubtedly, the biotech sector also experienced major pressure from private and public capital markets, and the sector was not rewarded for the years of work that management teams and their investors had put into the development of broad pipelines. Therefore, IPOs, if they happened at all, were valued often only slightly above the last private financing round and became financing transactions rather than being an exit. Less money from private and public investors was flowing into the sector. The biotech industry – and above all the venture capital firms – needed to develop new models to finance early-stage development assets. Their limited partners were not willing to accept the overall risks connected to drug development any longer and wanted to see higher capital efficiency, as well as decreased holding periods. TVM Capital Life Science and others started to think about new models of financing life sciences innovation, finding ways of managing drug development in a significantly more cost-effective development setup and governing the necessary development steps in a very different setting. This idea was fuelled by a growing perception on the part of the big pharmaceutical players that their in-house capacity for innovation was not increasing fast enough to fill a widening gap in their products pipelines related to an upcoming patent cliff which significantly would affect overall sales.



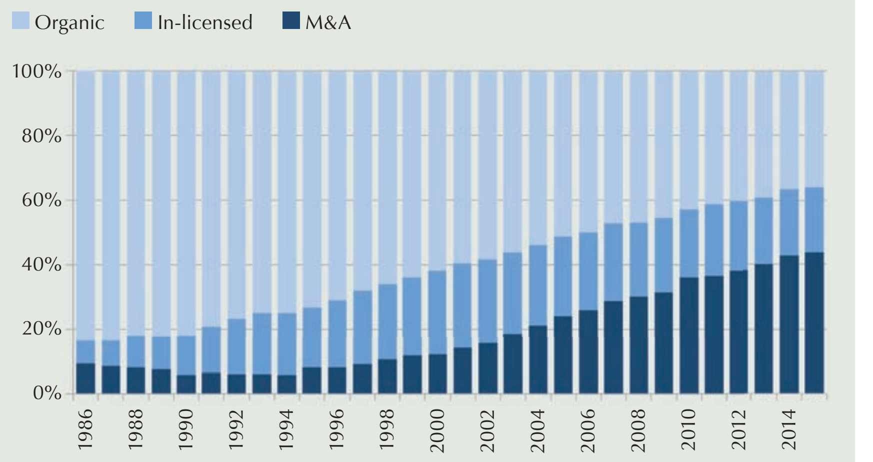
Source: TVM Capital Life Sciences Venture Capital

Successful TVM Capital Life Science exits 2000–2018

The investment case in biotech as of today

Global health care expenditures are projected to reach US$8.7tn by 2020, from

Picture: TVM



External innovation now accounts for over 60% of the combined sales of the top 25 companies.

Source: TVM Capital Life Sciences Venture Capital

Combined sales of current top 25 pharma companies

US$7tn in 2015. Growth is driven by improving treatments in key therapeutic areas coupled with rising labour costs and an increased life expectancy. North America, Western Europe, China, and Japan continue to be the largest healthcare markets. As populations age, healthcare will take an ever-larger share of GDP. Urgent unmet medical needs, the need of pharma and big biotech to diversify pipelines through acquiring external innovation, and the promise for high rewards generated by successful drug development projects have the potential to generate good return for all stakeholders: investors, founders, industry, and patients.

Although pharma companies continue to deal with the repercussions of patent expiries and payers' cost control efforts, the growing acceptance of innovative drugs that are either first-in- class or best-in-class, offering clear clinical benefits, are expected to drive sales growth for the next several years. Sales are expected to grow at an average of 4.4% annually to total projected US$1.2tn in 2020. Sales from the top 10 pharmaceutical companies account for ~35% of the global pharma market today. Scientific progress, general increased levels of education, and a more empowered patient population are driving changes in healthcare towards a more personalized experience that demands meaningful health outcomes as the core metric. However, despite the anticipation for steady and long-term growth, the industry faces several inherited challenges.

R&D spending grew from US$0.5bn per new drug approval in the mid-1990s to up to US$2.5bn today (this includes the cost of the pipeline products that failed). National reimbursement and insurance policies are increasingly incentivizing the prescription of less costly generic drugs after patent expiration. Pharma is also aiming at a rather narrow set of indications driven by blockbuster economics (>US$1bn in annual revenues). This is in stark contrast with the actual industry average for pharma products of US$522m five years post launch. Within the next five years, until 2022, current annual sales of approximately US$160bn will be at risk due to patent expirations. The industry will face mounting price pressure driven by governments seeking to control healthcare costs.

A new mode of action to successfully finance innovation in biotech

At TVM Capital Life Science a new mode of action of investing in early-stage drug development – as well as later-stage platform and medical technology companies – was installed to handle the above-mentioned requirements and challenges. The company invests in early-stage drug development projects and chaperons them to Proof-of-Concept (PoC) with a team of serial entrepreneurs and advisors and external providers for full-service R&D, specializing in lean development to PoC. This approach ensures reduced timelines and cost while providing big pharma quality for the produced clinical data. We offer our early-stage investees a majority stake outlining a clear path to exit. The management teams, founders, or originators of such projects will benefit from a reliable in-going and out-going equity participation as the capital required to exit is committed upfront and does not depend on future financing rounds with unpredictable dilutive effects. Ensuring exit at reach of PoC requires a highly skilled investment team with expert knowledge of the pharmaceutical industry's future demands. Also, the mitigation of investment risks in this setting is happening within the respective fund, not within the investee company as was the case in the early days of biotech investing. This shift required a new thinking and a new skillset in the investment team; the firm also built up an experienced operational team that can meet the challenges and is very deeply integrated into the global pharmaceutical industry. Now, after a couple of years, the investment firm prides itself on the smooth transition into this new mode of action. The company's recent exit of AurKa Pharma to Eli Lilly is a rewarding proof of the investment rationale.

However, it is important to say that this mode of action is not applicable to companies developing a platform technology, or companies offering innovation within the segments of medical technology or e-health. TVM Capital Life Science continues to invest in promising companies in these segments but will apply a later-stage, minority investment approach in these cases. Again, from the experience of the company's current investment activities, it is felt that this two-pronged investment strategy currently is the path of success for a life sciences dedicated venture capital firm like TVM – the emphasis being on 'currently.' ■

Picture: TVM

"Liquidity is key"

ONCOLOGY Roche's US arm Genentech has secured access to Affimed NV's ROCK platform to add multivalent antibodies to its cancer pipeline. These antibodies engage both NK cells and T cells of the innate and adaptive immune system, respectively. Affimed CEO Adi Hoess talks with EuroBiotech about the US$5bn deal and about Affimed's financing history.

EuroBiotech_Genentech is paying US$96m upfront and up to US$5bn, depending on the progress of the collaboration, plus royalties. How did Affimed manage to bag that deal without giving away its clinical-stage lead assets?
Hoess_*The collaboration we were able to make with Genentech was much bigger than we initially envisioned. Serious partnering discussions started in early 2018 but clinical data we presented some months ago clearly helped to accelerate the process. Most investors are interested in companies that develop products. As the value of the company is calculated almost exclusively based on the proprietary drug pipeline, it was important for us to keep the rights for our lead programmes AFM13 and AFM11. That we could sign such a sizable deal indeed was a bit stunning to investors. But as Affimed has shown various times in the past, our technology can generate a significant number of molecules that activate NK cells. And it is these molecules Genentech is interested in to complement its immunooncology pipeline.*

EuroBiotech_Since the announcement of the Genentech partnership Affimed's stock has tripled. With a market capitalization of US$300m, is there still some near-term upside potential?
Hoess_ *We believe there is continued upside as, our lead candidate AFM13 showed encouraging efficacy data in two indications: Hodgkin's lymphoma and T cell lymphoma. After early clinical data in a monotherapy as well as in a combination therapy setting, we now expect updates on these two AFM13 studies later this year. Together with our partner University of Texas MD Anderson Cancer Center, we will present preclinical data from a project combining AFM13 with adoptive NK cell transfer.*

DR. ADI HOESS began his biotech career at Morphosys AG as a scientist. The German native later became Director of Business Development. After Morphosys, he was Chief Commercial Officer at Jerini AG and CEO of Jenowis AG. In 2010, Hoess joined Affimed. Since 2011 he has been the company's CEO.

EuroBiotech_And what about the two companies Amphivena and Abcheck where Affimed owns 18.5% and 100% stakes, respectively?
Hoess_*Abcheck is extremely important from a strategic point of view but I don't see it as a value driver. The Czech company is an expert in antibody-binding domain generation. Developing a product in acute myeloid leukaemia – a very important indication – Amphivena is different. Affimed might be assigned a fraction of the value of Amphivena either when the company is acquired for a certain amount of money, or when differentiating clinical data is generated. At this stage, it's difficult to set a value for the Phase I asset. But seeing fewer toxicity issues compared to competing bispecific antibody drugs, we are confident that Amphivena has a promising candidate.*

EuroBiotech_Affimed is based in Heidelberg, Germany. To be listed on the US stock exchange Nasdaq, a Dutch holding company was created. Do you recommend this strategy?
Hoess_*The German law comes with some restrictions that are not ideally compatible with a biotech company – especially regarding access to capital. Other than the German AG, the Dutch NV allows us to operate like a US Inc. The structure allows US investors to be easily investible in Affimed. It's a working template that is reproducible in a straightforward fashion. As US investors can focus on so many companies listed on their stock exchanges, they are less likely to look in detail at European companies. So for easier access to US capital your company is better listed in the US. Additionally, there's a liquidity issue. The Affimed stock shows a high daily trading volume. Smooth investing and divesting in a stock is important for US short-term traders. If only a few hundred shares of a company are traded every day – as is the case for many Affimed-sized biotech companies listed on European stock exchanges – that's not going to work for these investors.* ■

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Picture: Affimed

Diversifying into oncology if ROI on bugs is too low

OLAV ZILIAN Senior Healthcare Analyst, Mirabaud Securities_ Big Pharma's interest in R&D on anti-infectives declined when other areas like oncology began offering higher returns. A few biotechs mirror pharma (Basilea, Idorsia and Polyphor), but could stay hidden gems.

As with other economic sectors, cyclicality is also seen in biopharmaceuticals, though over a longer period of time. A prevailing megacycle of today's healthcare industry is found in the expanding oncology market. Key drivers for its lasting and far-reaching growth are increasingly personalised treatment regimens, triggered by a series of innovations including: 1) diagnostic tests for biomarkers, or direct tumour sequencing; 2) an increasing number of drugs selectively targeting vulnerable points of tumours; 3) novel means to mobilize the immune system against cancer cells like checkpoint inhibitors. At the same time, these novel cancer drugs are more profitable due to a double multiplier, i.e. prolonged survival entails longer treatment multiplied by the lifted price point that is justified by the drugs' improved risk-benefit ratio.

Novel antibiotics, by contrast, were expected to provide higher returns on R&D, which eventually couldn't be met because: 1) diagnostics for identifying the causative microbe take too long vs the quick manifestation of the infection thus putting the patient's life at risk; 2) some infections are caused by more than a single agent; 3) under all these premises, broad spectrum antibiotics continue to prevail over novel narrow spectrum drugs; 4) despite their truly curative benefit, the price of antibiotics remains low.

What has been the consequence of the diverging economics of both therapeutic areas? Big Pharma's original enthusiasm reverted into deprioritizing R&D on antibiotics, e.g. in favour of oncology. By contrast, only a few biotechs initiated such a reversal, but investors do not necessarily welcome such a move. They could be hidden gems if their valuation is depressed. Swiss Basilea is a prime example: its pipeline has been consistently expanded into oncology, starting ten years ago, yielding BAL101553 (now in Phase II for glioblastoma and ovarian cancer); BAL3833 (in Phase I); and in-licensed derazantinib (in pivotal Phase II for intrahepatic cholangiocarcinoma); while the antibiotic Zevtera (approved in the EU; US Phase III ongoing) and the antifungal Cresemba (approved in the US and EU) are being commercialized by various distributors (e.g. Correvio and Hikma) and partners (e.g. Astellas and Pfizer) in an increasing number of markets. Convincing clinical trial success is needed to see companies like Basilea, Idorsia, and Polyphor properly valued, a breakthrough in oncology could be an occasion. ■

News from the floor

VECTURA GROUP PLC *JPMorgan Chase & Co. restated their overweight rating on shares of Vectura Group (LON:VEC) in a report issued in August. They currently have a GBX140 price objective on the stock that traded around GPX90 all summer.*

OXFORD BIOMEDICA PLC *The lentivirus vector platform company's stock (LON:OXB) had its "buy" rating reiterated by equities research analysts at Peel Hunt in a research report issued in late August. After a Parkinson's Disease deal with Axovant in June, the stock soared to more than GBX1,060 but later normalized to around GPX850.*

EVOTEC AG *German biopharma play Evotec (ETR:EVT) has been given a €26.00 price target by Oddo BHF in September. The price target suggests a potential upside of 17.75%. After sealing the third drug discovery deal with Celgene (US) and another one with Centogene (Germany) in rare diseases, Evotec's stock had hit an all-time high of €23.36 in early September.*

ZEALAND PHARMA A/S *Needham & Company LLC set a US$26.00 price objective on Danish peptide drug developer Zealand Pharma (NASDAQ:ZEAL) in a research report released in August. The brokerage currently has a "buy" rating on the stock.* ■

COMPANY	QUOTE	M-CAP	52 WEEKS INDICATOR low high
4D Pharma plc	2.10	140,000k	
4SC AG	3.61	110,000k	
A1M Pharma AS	0.44	3,600k	
AB Science SA	4.25	170,000k	
AB-Biotics SA	3.32	41,000k	
Abcam plc	15.42	2,900,000k	
Abivax SA	7.55	74,000k	
Abzena plc	0.17	37,000k	
Active Biotech AB	0.36	53,000k	
Addex Therapeutics Ltd	2.17	62,000k	

European Biotechnology

European Biotech Stocks

The unique and most complete list of share price developments of biotech companies listed in Europe – exclusively in European Biotechnology Magazine.

COMPANY	QUOTE	M-CAP	52 WEEKS INDICATOR
ADL Bionatur Solutions SA	2.06	80,000k	
Adocia SAS	16.84	120,000k	
Advicenne SACA	12.0	97,000k	
ALK-Abelló A/S	153.42	1,700,000k	
Allergy Therapeutics plc	0.27	170,000k	
Alligator Bioscience AB	3.08	210,000k	
Annexin Pharmaceuticals AB	0.36	6,400k	
Aqua Bio Technology ASA	0.31	2,200k	
Argenx SE	78.20	2,500,000k	
Arocell AB	0.43	17,000k	
Asit Biotech SA	3.10	54,000k	
Avacta Group plc	0.31	35,000k	
Avantium Holding NV	5.65	150,000k	
Basilea Pharmaceutica AG	53.26	630,000k	
Bavarian Nordic A/S	24.78	800,000k	
Bergenbio ASA	3.72	190,000k	
Bioarctic AB	10.79	950,000k	
Bio-On SpA	55.90	1,100,000k	
Biocartis NV	12.20	630,000k	
Biofrontera AG	5.94	270,000k	
Biogaia AB	48.05	830,000k	
Bioinvent International AB	0.24	85,000k	
Biomed-Lublin SA	0.27	17,000k	
Biomérieux SA	76.30	8,900,000k	
Biophytis	2.23	31,000k	
Bioporto Diagnostics A/S	0.46	69,000k	
Biosearch Life SA	1.68	97,000k	
Biotec Pharmacon ASA	0.50	24,000k	
Bioventix plc	36.48	190,000k	
Biovica International AB	1.02	19,000k	
Bone Therapeutics SA	9.40	72,000k	
Brain AG	18.32	320,000k	

COMPANY	QUOTE	M-CAP	52 WEEKS INDICATOR low high
C4X Discovery Holdings plc	1.02	47,000k	
Calliditas Therapeutics AB	5.35	190,000k	
Cantargia AB	1.98	130,000k	
Carbios SAS	8.84	40,000k	
Cassiopea SpA	53.26	530,000k	
Cellectis SA	23.02	970,000k	
Cellink AB	12.95	110,000k	
Celon Pharma SA	7.69	350,000k	
Celyad SA	24.50	290,000k	
Cerenis Therapeutics SA	1.91	36,000k	
Circassia Pharmaceuticals plc	0.81	290,000k	
Co.don AG	5.85	120,000k	
Cosmo Pharmaceuticals NV	123.76	1,900,000k	
Curetis AG	3.45	57,000k	
Cytotools AG	9.24	19,000k	
Cyxone AB	0.52	10,000k	
DBV Technologies SA	37.88	1,200,000k	
Deinove SA	2.30	35,000k	
Destiny Pharma plc	1.01	44,000k	
Diamyd Medical AB	0.70	39,000k	
Diasorin SpA	87.40	5,000,000k	
Elanix Technologies AG	3.01	23,000k	
e-Therapeutics plc	0.09	25,000k	
Ellen AB	0.02	4,700k	
Enzymatica AB	0.29	21,000k	
Epigenomics AG	2.11	52,000k	
Erytech Pharma SA	8.81	160,000k	
Esperite NV	0.25	8,900k	
Eurobio Scientific SA	4.43	44,000k	
Eurofins Scientific SE	466.20	8,300,000k	
Evgen Pharma plc	0.18	17,000k	
Evolva SA	0.26	200,000k	
Evotec AG	21.32	3,200,000k	
Expedeon AG	1.34	69,000k	
Expres2ion Biotech Holding AB	1.13	14,000k	
Faron Pharmaceuticals Oy	1.25	39,000k	
Fermentalg SA	3.08	53,000k	
Fit Biotech Oy	0.0	1,400k	
Formycon AG	30.95	280,000k	
Fusion Antibodies Ltd.	0.81	18,000k	
Gabather AB	1.36	7,100k	
Galapagos NV	83.0	4,200,000k	
Genedrive plc	0.31	5,800k	
Geneuro SA	5.60	82,000k	
Genfit SA	22.74	700,000k	
Genmab A/S	140.34	8,800,000k	
Genomed SA	5.11	7,100k	
Genomic Vision SA	0.90	6,400k	
Genovis AB	0.59	37,000k	
Genoway SA	1.92	11,000k	
Gensight Biologics SA	2.17	54,000k	
Genkyotex SA	1.47	110,000k	
Genus plc	27.79	1,700,000k	
Global Bioenergies SA	13.98	63,000k	
Hansa Medical AB	24.72	940,000k	
Heidelberg Pharma AG	2.75	77,000k	
Herantis Pharma Oyj	7.20	35,000k	
Hofseth Biocare ASA	0.27	75,000k	
Horizon Discovery Group plc	2.52	370,000k	

COMPANY	QUOTE	M-CAP	52 WEEKS INDICATOR low high
Hvivo plc	0.70	56,000k	
Hybrigenics SA	0.48	22,000k	
Idorsia Ltd.	21.71	2,800,000k	
Immunicum AB	0.73	37,000k	
Immunodiagnostic Systems plc	2.57	74,000k	
Immunovia AB	17.39	330,000k	
Immupharma plc	0.19	28,000k	
Index Pharm. Holding AB	0.65	41,000k	
Infant Bacterial Therapeutics AB	18.37	210,000k	
Innate Pharma SA	4.58	260,000k	
Integragen SA	2.07	14,000k	
Intervacc AB	0.90	34,000k	
Inventiva SA	8.52	190,000k	
Isofol Medical AB	3.12	99,000k	
ISR Holding AB	0.41	7,700k	
Kancera AB	0.10	19,000k	
Karo Pharma AB	3.27	540,000k	
Kiadis Pharma BV	12.80	290,000k	
Kuros Biosciences AG	5.93	51,000k	
Lysogene SA	1.95	24,000k	
Mabion Ltd	26.13	360,000k	
MDxHealth SA	2.86	160,000k	
Medical Prognosis Institute A/S	1.21	30,000k	
Medigene AG	12.56	310,000k	
Medivir AB	3.98	95,000k	
Mereo Biopharma Group plc	3.09	220,000k	
Metabolic Explorer SA	1.99	47,000k	
Midatech Pharma plc	0.29	19,000k	
Molecular Partners AG	17.64	370,000k	
Molecular Medicine SpA	0.40	190,000k	
Mologen AG	4.89	37,000k	
Morphosys AG	94.65	3,000,000k	
Motif Bio plc	0.36	110,000k	
Nanobiotix SA	17.60	340,000k	
NEL ASA	0.37	400,000k	
Neol Biosolutions SA	0.25	2,300k	
Neovacs SA	0.31	29,000k	
Neuron Biopharma SA	0.30	4,900k	
Neurosearch A/S	0.62	15,000k	
Neurovive Pharmaceutical AB	0.40	37,000k	
Newron Pharmaceuticals SpA	9.11	160,000k	
Nicox SA	7.75	230,000k	
Nordic Nanovector ASA	5.67	270,000k	
Novozymes Biopharma DK A/S	46.67	13,800,000k	
Noxxon Pharma NV	2.58	10,000k	
Nuevolution A/S	1.59	79,000k	
Oncimmune Holdings plc	1.28	79,000k	
Oncoarendi Therapeutics SA	5.46	72,000k	
Oncodesign Biotechnology SA	10.35	71,000k	
Oncopeptides AB	14.44	630,000k	
Onxeo SA	1.09	56,000k	
Optibiotix Health plc	1.17	98,000k	
Orphazyme A/S	9.88	190,000k	
Oryzon Genomics SA	4.04	140,000k	
OSE Pharma SA	3.98	58,000k	
Oxford Biodynamics plc	2.35	220,000k	
Oxford Biomedica plc	9.09	600,000k	
Oxurion NV	6.84	260,000k	
Paion AG	2.27	150,000k	

COMPANY	QUOTE	M-CAP	52 WEEKS INDICATOR low high
PCI Biotech Holding ASA	3.60	92,000k	
Pharma Mar SA	1.58	350,000k	
Pharming Group NV	1.25	770,000k	
Pharnext SA	10.45	120,000k	
Photocure ASA	6.18	130,000k	
Physiomics plc	0.05	3,700k	
Plant Advanced Technologies SA	23.0	21,000k	
Polyphor AG	29.44	320,000k	
Poxel SA	6.63	170,000k	
Premaitha Health plc	0.12	47,000k	
Probi AB	41.03	480,000k	
Probiodrug AG	3.03	24,000k	
Promore Pharma AB	1.45	29,000k	
Proteome Sciences plc	0.04	13,000k	
Qiagen NV	32.93	7,500,000k	
Quantum Genomics SAS	1.75	20,000k	
Relief Therapeutics Holding AG	0.01	12,000k	
Reneuron Group plc	0.94	30,000k	
Salvarx Group plc	0.85	31,000k	
Saniona AB	3.33	74,000k	
Santhera Pharmaceuticals AG	14.74	95,000k	
Sareum Holdings plc	0.01	24,000k	
Scancell Holdings plc	0.13	53,000k	
Selvita SA	11.65	190,000k	
Sensorion SA	2.86	37,000k	
Shield Therapeutics plc	0.35	40,000k	
Silence Therapeutics plc	1.93	130,000k	
Simris Alg AB	0.71	6,800k	
Skinbiotherapeutics plc	0.23	28,000k	
Stallergenes Greer plc	28.50	560,000k	
Summit Therapeutics plc	0.41	33,000k	
Swedish Orphan Biovitrum AB	25.54	7,100,000k	
Synairgen Research Ltd	0.22	20,000k	
Targovax ASA	1.13	56,000k	
Theradiag SA	1.47	13,000k	
Theranexus SADIR	14.64	46,000k	
Tissue Regenix Group plc	0.10	120,000k	
Tiziana Life Sciences plc	1.11	140,000k	
Transgene SA	2.98	190,000k	
Txcell SA	2.42	56,000k	
Valirx plc	0.03	11,000k	
Valneva SE	3.95	310,000k	
Vectura Group plc	0.82	550,000k	
Veloxis Pharmaceuticals A/S	0.13	230,000k	
Vernalis plc	0.07	36,000k	
Verona Pharma plc	1.34	140,000k	
Virogates A/S	10.59	34,000k	
Vita 34 AG	14.60	61,000k	
Xbrane Biopharma AB	5.44	34,000k	
Xintela AB	0.31	9,500k	
Zealand Pharmaceuticals A/S	14.08	450,000k	

All quotes are listed in euro. All data is provided without guarantee. The effective date is 10 September 2018.
These dedicated biotech companies are listed on European stock markets.