6th Analysis of European Biotech Companies on the Stock Markets: US versus Europe

Destination Growth
CONSULTANCY & RESEARCH

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Executive Summary

After a healthy reset in 2016, biotech stock markets experienced a new wave of optimism with increased volumes of IPOs and financings in 2017. Investors’ appetite was revived on the US Nasdaq in particular. This report highlights the key facts.

Compared to the more cautious situation in 2016, the European public biotech sector is on the road to further growth this year. In 2017, the volumes of IPOs and follow-on financings increased compared to the preceding year. This is demonstrated by the final numbers for 2017, brought together in this issue of BIOCOM’s capital market report.

The report analyses all of the European biotech firms listed on one of the 14 trading centres in Europe or on the US Nasdaq. Taking all indicators into account – number and volumes of IPOs, follow-on financings and secondary listings – total proceeds of €5.09bn were raised by European biotech firms in 2017, an increase of 54% compared to 2016. In 2017, a total of 19 European biotech IPOs took place, raising a total amount of €815m. This year shows an increase of 47% compared to the same period in 2016.

Most of the 19 firms opted for one of the 14 European trading centres, with three companies floating on US Nasdaq, instead. The highest IPO volumes in 2017 were recorded for ObsEva SA (€90m), InflaRx (€86m) and Nucana Biomed (€85m) on the US Nasdaq. Additionally, five secondary listings of European companies on Nasdaq were recorded to date: argenx (€103m), Verona Pharma (€82m), Zealand Pharmaceuticals (€67m), ERYtech (€106.5m) and Ablynx (€195m).

Revival on the US Nasdaq

In 2017, US investors showed significant interest in biotech stocks compared to the preceding year. European biotech companies profited from this positive trend. They raised total financial proceeds of €2.16bn via IPOs, secondary listings and follow-on financings in the US, representing almost half (42%) of the total capital raised by all European biotech companies in 2017.

Europe more attractive in 2017

In 2017, the majority of companies decided on a listing in Europe (15) in comparison to the US (4). Among the European trading centres, Paris and London, in particular, are the most attractive stock markets. In addition, the stock market in Stockholm seems to appeal to more and more biotech companies.

Key facts of the European public biotech sector

- 233 public biotech companies with €155.05bn market cap*
- 35 European biotech companies listed on US Nasdaq
- 19 IPOs with €815m capital raised in 2017 (+47%)
- 122 financings with €4.27bn capital raised in 2017 (+56%)
- Total financing proceeds of €5.09bn in 2017 (+54%)

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*Market cap on 4 Oct 2017
## Capital raised by European biotech companies on the stock markets*

<table>
<thead>
<tr>
<th>Stock market segment</th>
<th>2016</th>
<th>2017</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Capital raised via IPOs</td>
<td>Capital raised via follow-ons</td>
</tr>
<tr>
<td>Euronext</td>
<td>€127.5m</td>
<td>€1,083.0m</td>
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<tr>
<td>Euronext Grow</td>
<td>€1,210.5m</td>
<td>–</td>
</tr>
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<td>Alternative Investment Market (AIM)</td>
<td>€37.9m</td>
<td>€235.1m</td>
</tr>
<tr>
<td>LSE Main</td>
<td>–</td>
<td>€33.9m</td>
</tr>
<tr>
<td>Madrid</td>
<td>€16.8m</td>
<td>–</td>
</tr>
<tr>
<td>Nasdaq Nordic Main Market</td>
<td>€98.9m</td>
<td>€321.3m</td>
</tr>
<tr>
<td>Nasdaq Nordic First North</td>
<td>€38.4m</td>
<td>€98.2m</td>
</tr>
<tr>
<td>Frankfurt Stock Exchange (FSE)</td>
<td>€31.5m</td>
<td>€199.1m</td>
</tr>
<tr>
<td>Swiss Exchange (SIX)</td>
<td>–</td>
<td>€28.6m</td>
</tr>
<tr>
<td>Oslo Børs</td>
<td>€118.3m</td>
<td>–</td>
</tr>
<tr>
<td>Warsaw Stock Exchange (WSE)</td>
<td>–</td>
<td>€57.5m</td>
</tr>
<tr>
<td>US Nasdaq</td>
<td>€164.6m</td>
<td>€189.7m</td>
</tr>
</tbody>
</table>

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*Capital raised by companies which are traded in Europe and the US is assigned individually where the financing round took place.
Key Facts for 2017
New Wave of Optimism

Following a more cautious year 2016, the European public biotech sector observed an new increase of IPO and follow-on financing volumes in 2017. Riding on the wave of this development, new found confidence is growing.

After record financings for European biotech companies on the stock market in 2015 and significantly lower activity in 2016, there is currently a growing optimism that sees stock markets as a viable route for biotech companies to access further capital. According to the analysis, which also includes all European biotech firms listed on the US Nasdaq, all of the key figures for 2017 show new signs of confidence. The 233 European biotech companies raised a total of €5.09bn of financial proceeds until the end of 2017 – 54% more than in the same period of time in 2016 (€3.30bn) (see fig. 2, p. 9).

**IPO window open**

In 2017, a total of 19 European biotech IPOs took place, raising a total figure of €815m. This year shows an increase of 47% on the same period in 2016 (see Fig. 5, p. 10). The majority of 15 firms opted for one of the 14 European trading centres, with four firms floating on US Nasdaq, instead. Compared to the previous year, investor appetite was higher and the sums larger. The greatest IPO volumes in 2017 were recorded for ObsEva SA (€90m), InflaRx (€85m) and Nuca-na Biomed (€86m) on the US Nasdaq.

Currently, the most attractive stock market locations are Paris (47) and London (44). However, the number of listed biotech companies in Sweden has also increased by up to 41. The shares of 35 European companies are currently traded on US Nasdaq and the most recent US IPO was conducted by German InflaRx (€86m).

**Follow-on financings**

In 2017, investors are showing increased enthusiasm for European biotech companies compared to 2016. Until the end of 2017 a total of €4.27bn was dropped into these companies via follow-on financings, a substantial increase of 56% compared to 2016. The average size of capital increase in 2017 almost doubled to €35m, compared to €19m in the same period of 2016. Much of the increase is due to the fact, that the climate on Nasdaq ameliorated significantly whereas on the European trading centres almost the same money was raised with less follow-on financings taking place in 2017 (122) compared to 2016 (144). Within Europe, Euronext demonstrated the most activity with 33 financings and total proceeds of €1.4bn, followed by Frankfurt (22 financings, €284m).
Key facts of European and US public biotech sectors

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<thead>
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<th></th>
<th>Europe</th>
<th>US</th>
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<tbody>
<tr>
<td>Number of public biotech companies</td>
<td>233</td>
<td>331(\frac{1}{2})</td>
</tr>
<tr>
<td>Market capitalisation*</td>
<td>€155.05bn</td>
<td>–</td>
</tr>
<tr>
<td>Turnover (2016)</td>
<td>€16.07bn</td>
<td>–</td>
</tr>
<tr>
<td>Capital raised via IPOs</td>
<td>€815m</td>
<td>€2.01bn(\frac{1}{2})</td>
</tr>
<tr>
<td>Number of IPOs</td>
<td>19</td>
<td>26(\frac{1}{2})</td>
</tr>
</tbody>
</table>

Source: ¹US companies on Nasdaq US, ²BIOCOM research based on data provided by investships.com
³Market cap on 4 Oct 2017

Compared to last year’s analysis, investors demonstrated improved interest in the companies in Europe and for this reason, they observed a slight increase in their overall market cap (2016: €106bn).

**Market cap**

The European public biotech sector continues to mature. At the beginning of October 2017, the European biotech companies had a joint market capitalisation of €155bn. About 40% of the European biotech companies operate in the “micro” range between US-$50m and US-$300m (see Fig. 1). A further 31% ranks among nano caps (below US-$50m). Therefore, 71% of all companies have a market cap of less than US-$300m. A total 17 companies have caps exceeding US-$2bn, these include the firms Actelion, Novozymes, Qiagen, Genmab and Eurofins.

and AIM (16 financings, €231m). A significant increase was observed in the US where a total of €1.83bn came in through Nasdaq. This was almost ten times as much as in 2016 (€190m).
Oncology in the spotlight
The dominance of nano and micro cap companies in Europe also explain the comparatively low turnover. In 2016, European biotech firms generated a combined total turnover of €16.07bn (2015: €14.02bn). 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. Almost all of the 19 stock market newcomers in 2017 can be assigned to this category. The most attractive field within the health area is oncology (see Fig. 4). A total of 75 companies operate in this field, followed by neurology (36), inflammatory (31) and metabolic diseases (30) 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 13 companies overall operate in this field. Another area of listed European companies is industrial
A total of 20 firms are involved in the development of new enzyme-based processes or biobased solutions for various industries. German bioeconomy pioneer Brain AG has been among the newcomers in this field in 2016. In 2017, Swedish SenzaGen, a specialist for immunotoxicological assays to predict and classify chemical sensitizers with a state-of-the-art predictive performance, went public in Stockholm.

Stockholm catches up

With 14 different trading centres, the variety of stock exchanges relevant for 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. In 2017, 5 IPOs took place here. However, Scandinavian city Stockholm has caught up with 6 new list-
ings recorded this year, among them Oncopeptides AB, raising €68m, and BioArtic NeuroScience AB with €71.8m (see Fig. 7). Two British newcomers – Destiny Pharma and SkinBio Therapeutics – performed an IPO at the LSE. One listing each took place in Oslo (BerGenBio) and in Copenhagen (OrphaZyme). The 5 companies already listed, Zealand Pharmaceuticals (Nasdaq Nordic), argenx (Euronext), Verona Pharma (AIM), ERYtech Pharma (Euronext) and Ablynx (Euronext), went public with a secondary offering on Nasdaq in New York. As forecast by analysts, the overall mood on the stock markets improved compared to the previous year. The number and volumes of IPOs as well as follow-on financings increased (see Fig. 8+9), in particular due to an upward trend on Nasdaq. It seems, that IPOs and stock market listings are increasingly establishing themselves as one of financing options to strengthen future business growth in the European biotech sector.

Fig. 8: Development of follow-on financings in €bn since 2012

Fig. 9: Development of IPO activity and volumes in €m since 2012
Focus on US Nasdaq
US Market Revival

Biotech stocks in the US have recovered significantly in 2017. It corresponds with a number of successful initial public offerings, secondary listings and substantial follow-on financings by European biotech companies.

The global public market surge in 2014 was followed by an all-time high for biotech companies on the US stock markets and European biotech firms showed huge interest in opting for a US listing. However, in 2015 the situation started to change and the biotech IPO boom began to cool off. In 2016, matters deteriorated even further. Now, in 2017, the situation has finally improved as the US stock market offers a far greater number of biotech investors than their European counterparts. For this reason, European biotech companies haven’t lost their interest in IPOs and secondary listings abroad. In total, 35 European biotech companies were listed on Nasdaq by the end of 2017.

Investors’ appetite returns

In 2017, investors showed significant interest in biotech stocks compared to 2016. European biotech companies profited from this trend. They raised total financial proceeds of €2.16bn via IPOs, secondary listings and follow-on financings on the US Nasdaq. This is nearly half (42%) of the total capital raised by all European biotech companies in 2017 and highlights the power of biotech-focused investors available through Nasdaq.

US boasts greater IPO volumes

In 2017, 4 European biotech companies raised a total of €324m via IPOs on the US Nasdaq, which is almost twice as much (+97%) compared to 2016 (€164m) and includes Swiss company ObsEva SA (€90m), German InflarX (€85.8m) and UK-based Nightstar Therapeutics (€63.5m) and Nuca-na Biomed (€64.7m). In the US, average IPO volumes are higher than those on European stock exchanges. In 2017, the US stock exchange average amounted to €81m, almost 60% more than that of European exchanges (€32.7m). The Nasdaq proceedings, however, didn’t top past IPO levels, such as those of UK-based Adaptimmune (€170m) in 2016 or Forward Pharma (€186m) from Denmark in 2014.

Follow-on financings

US investors’ appetite was revived in 2017 following a decline in 2016. The 35 listed companies attracted a combined total of €1.83bn in follow-on financings (see Fig. 12, p. 15), including 5 secondary listings which alone amounted to a total capital of €553.3m. Compared to their counterparts which are listed on European stock exchanges only, the firms on the US Nasdaq generated significantly more
capital this year and with greater average volumes (US: €81m vs. Europe: €32.7m).

Drug developers aim for US Nasdaq
Drug developers, in particular, opt for a US listing, which is clearly associated with their high demands for capital. Newcomers to the Nasdaq in 2017 are active in the field of reproductive health (ObsEva), cancer therapeutics (Nucana Biomed), blinding eye diseases (Nightstar Therapeutics) and inflammation (InflarX). The same applies for the secondary listings: respiratory diseases (Verona Pharma), metabolic diseases (Zealand Pharmaceuticals) and cancer/autoimmune diseases (argenx, ERYtech, Ablynx).

Fig. 10: Comparison of capital raised via IPOs in €m and number of IPOs

<table>
<thead>
<tr>
<th>Year</th>
<th>Nasdaq US listing</th>
<th>Listing in US/Europe</th>
<th>Listing in Europe</th>
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<tbody>
<tr>
<td>2017</td>
<td>324.0</td>
<td>553.3</td>
<td>490.7</td>
</tr>
<tr>
<td>2016</td>
<td>391.3</td>
<td>470</td>
<td>406.6</td>
</tr>
<tr>
<td>2015</td>
<td>406.6</td>
<td>506.9</td>
<td>740.0</td>
</tr>
<tr>
<td>2014</td>
<td>506.9</td>
<td>806.2</td>
<td>806.2</td>
</tr>
<tr>
<td>2013</td>
<td>59.4</td>
<td>47.0</td>
<td>47.0</td>
</tr>
<tr>
<td>2012</td>
<td>110.1</td>
<td>94.0</td>
<td>94.0</td>
</tr>
</tbody>
</table>
Greater market capitalisation

In 2017, 15% of the 233 listed companies traded their shares on the US Nasdaq. The companies have a combined market capitalisation of €32.19bn, which means an average of €975m. This is almost one third higher (€630m) than the market cap of the firms listed in Europe only. As seen in Fig. 11, the lion’s share of US-listed companies (48.5%) operate in the small-market capitalisation range between US-$300m and US-$2bn with a further 36.4% of the firms within a micro cap range between US-$50m and US-$300m. Similar to their European-listed counterparts, only a few companies (15.2%) fit in the mid-market cap range between US-$2bn and US-$10bn. A big difference between both markets, however, is that in the US there are no companies in the nano-market cap below US-$50m. This suggests that the US-listed companies have a slightly higher degree of maturity.

Fig. 11: Comparison of market capitalisation

Fig. 12: Comparison of follow-on financings in €m

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The Analysts’ View
Big Winners and Promising Deals

In 2017, European biotech stock markets performed quite well although some big winners dominated the headlines. Large M&A deals provided notable returns for investors and many licensing deals generated significant alpha. *By Samir Devani*

Thus far in 2017*, European biotech stocks have outperformed broader market indices and the more defensive larger cap pharma sector as well as performing on a par with their US biotech counterparts. However, the heterogeneity of the sector means there are always some big winners and big losers!

**Several stock market winners**
Notable winners include German Evotec, with its shares up by approximately 150%, driven by its acquisition of Aptuit and the extension of its collaboration with Bayer. Finnish Faron Pharmaceuticals’ shares are up by over 200% year-to-date due to progress in its phase III trial for Traumakine in Acute Respiratory Distress Syndrome. Finally, Swedish Hansa Medical has seen its shares rise by approximately 80% based on positive data from its lead drug, IDeS, being tested as a desensitisation treatment prior to kidney transplantations. So far year-to-date, Pharming from the Netherlands has been the top performer, with its share up by nearly 250% driven by a combination of a re-financing and a potentially earlier than anticipated submission of an Supplemental Biologics License Application (sBLA) for prophylactic use of Ruconest.

**Promising licensing deals**
Clinical data is a key driver of share prices for biotech stocks and even in risk averse periods it can generate significant alpha for investors. The other main driver for biotech stock prices are licensing deals – proving you have a valuable asset. So far this year, there have been big deals for Swiss Basilea (licensed Cresemba in Europe to Pfizer), Ablynx from Belgium (eight Nanobody-deal with Sanofi), and Danish Bavarian Nordic (licensed HfV-1 and hepatitis B vaccines to Janssen). The flip side is that the loss of a major partner can have a crushing impact on a share price as observed with French company Adocia, whose shares have fallen over 70% year-to-date following Lilly exiting its deal for BC Lispro.

“*The European biotech sector has lost its bellwether stock.*”

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* ANALYSIS OF EUROPEAN BIOTECH COMPANIES ON THE STOCK MARKETS: US VS EUROPE

*The Analysts’ View*
Muted IPO activity
From a funding perspective, thus far in 2017*, IPO activity remains relatively muted and at a similar level to 2016, although we note a significant number of new European IPOs originating from the Scandinavia region (e.g. BoneSupport, Oncopeptides, Isofol Medical, and BerGenBio). Appetite for secondary follow-on raises remained robust this year, although we note similar to last year the bigger raises were carried out in the US (Galapagos raised over US-$360 million and argenx over US-$100 million on Nasdaq). As we go to press, Ablynx has just completed its secondary listing on Nasdaq, raising US-$200 million.

CAR-T excitement in Europe
From a technology perspective, CAR-T has been hot for a while. Now, Swiss company Novartis’ and British-based Oxford Biomedica’s FDA approval for CTL019 now brings the first CAR-T therapy to market. Oxford Biomedica and Celyad, a Belgian firm, have been strong performers in 2017, having been seen as direct benefactors of excitement over CAR-T in Europe. Response rates using this platform have been outstanding, but durability and safety questions remain. This has not stopped Gilead, however, from offering US-$11.9 billion for fellow CAR-T therapy developer Kite Pharma in the US!

Outlook for 2018
For 2018, an environment in which global interest rates are rising may challenge equity market performance, which would clearly have a negative impact on the biotech sector subgroup, especially as the sector is high beta. While the drug pricing debate continues, the political charge appears to have receded, although payer-driven pricing pressure remains high. There continues to be lots of important company events to look forward to including:

1. a CHMP decision on Ablynx’s caplacizumab for the treatment of thrombotic thrombocytopenic purpura;
2. 24 week biopsy data from Summit Therapeutic’s ezutromid for Duchenne muscular dystrophy;
3. Phase I data from Valneva’s globally leading Lyme disease vaccine;
4. results from multiple Phase I studies of Celyad’s CAR-T CYAD-01;
5. Phase III results from Newron’s sarizotan for Rett syndrome; and
6. Phase III results from PharmaMar’s Zepsyre in ovarian cancer.

*Important notice: all data as of October 25th 2017
Prior to co-founding Rx Securities, Samir was a founding partner of Code Securities, a specialist life sciences investment bank which was formed in 2003, acquired by Nomura in 2005 and continued as Nomura Code Securities until late 2013. For many years, Nomura Code was the most active adviser in the European healthcare sector, measured by the number of transactions and equity capital raised. Samir has worked as a pan-European biotechnology equity research analyst for over 15 years. Prior to Nomura Code he held similar positions at Altium Capital, JP Morgan and Numis Securities. As well as advising institutional fund managers on their healthcare investments, he has significant secondary market fundraising and IPO experience. Samir is a registered pharmacist and completed a degree in Pharmacy at London University’s School of Pharmacy and a PhD in pharmaceutical technology at King’s College London.
Focus on Euronext
The Life Science Leader

Nearly a decade after the financial crisis, the European Life Science sector is flourishing again and has reached a momentum that was quite unforeseeable in the aftermath of 2008. In 2014 and 2015, companies reached a record high in matters of revenues, net income and initial public offerings (IPOs). Indeed, in 2014, more than 50% of European companies increased their R&D spending.

Euronext, which is based in France, Belgium, the Netherlands and Portugal, and since September 2017 is also present in Germany, Switzerland, Spain and Italy, has dedicated resources over the past five years to financing SMEs with a focus on Tech SMEs and in particular on Life Sciences. Euronext is committed to support the European Life Science industry and contribute towards their efforts to raise money and create jobs. This has been successful with 49 Life Sciences IPOs since 2013 on Euronext markets, making Euronext the listing venue of choice for the life science sector from domestic and non-domestic European countries.

Euronext is the largest Life Science stock market in Europe
During the 2013–2017 period, 48% of the 418 European Life Science companies which listed on markets decided to list their shares on Euronext. Capital raised via IPOs and follow-on financings on Euronext by European Life Science companies since 2013 amounts to €8.6bn. To date, Euronext has listed 88 life sciences companies – including 50 biotechs and 38 medtechs. These companies have a combined market capitalisation of €22.8bn.

Non-domestic companies chose Euronext
The sudden boost of the biotech sector in 2014, was seen on Euronext faster than on any other stock exchange. That same year, the German company Probiodrug listed and secured €22.5m (~$26m) on Euronext Amsterdam. Probiodrug develops drugs for Alzheimer’s disease and already has its lead candidate in phase 2 development. “We chose Euronext, as it has evolved into the leading European exchange and trading platform for technology companies, including those in the life sciences,” explains Konrad Glund, CEO. “Our IPO together with the follow-on financings, demonstrates the successful access to and acceptance of
Euronext Life Science overview*

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<table>
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<tbody>
<tr>
<td>Number of Life Science companies on Euronext</td>
<td>88</td>
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<tr>
<td>Market capitalisation</td>
<td>€22.8bn</td>
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<tr>
<td>Turnover (year-on-year)</td>
<td>€20.8bn</td>
</tr>
<tr>
<td>Capital raised via IPOs and FO since 2013</td>
<td>€8.6bn</td>
</tr>
<tr>
<td>Number of IPOs since 2013</td>
<td>49</td>
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</table>

*All data as of October 26th 2017

international investors. We have raised approximately €50m (~$59m) over the last three years.”

Geneuro is a Swiss company that focuses on diseases of the nervous system and autoimmune diseases. It listed in 2016 on Euronext Paris and raised €33m (~$39m) after its IPO. “Our domestic stock exchange is SIX,” explains Miguel Payró, CFO of Geneuro. “Here, there are very few listed biotechs and even less SMEs. There are also less funds and analysts following biotechs than on Euronext Paris, where the biotech ecosystem is much deeper and more dynamic.”

**TECH SME focus and solutions**

Euronext is conscious of the growth potential, funding requirements and sector-
specific needs of Tech companies. As a result, Euronext has been fine tuning initiatives that offer solutions, support and visibility to both non-listed and listed innovative European businesses. To date, among the 88 life sciences companies listed on Euronext, 84 are SMEs with an average market capitalisation of €263m.

In 2015, Euronext launched TechShare: a free educational programme to help Tech SMEs become acquainted with capital markets. TechShare equips Tech and Biotech entrepreneurs with the tools to best leverage capital markets and better understand market mechanics. While the 1st cohort (2015) of the one year-long programme welcomed 5 Life Sciences participants, this year’s program (3rd cohort) contains 15 Life Sciences companies.

Fig. 14: Geographic origin of Euronext’s investors

Source: Euronext

Fig. 15: Life Science listed companies per market cap range (€m)

Source: Euronext
Two participants of the 1st edition of Tech-Share have listed on our markets in 2017: Oasmiz in February, an SME specialised in “connected holidays” which raised €9m with an IPO market capitalisation of €22m, and Balyo in June, a business specialised in the automation of handling trucks, which raised €46m with an IPO market capitalisation of €109m.

Another solution created by Euronext is the Biotech Barometer, produced on a semester basis by Euronext and BiotechBourse. It provides the key trends and figures about Euronext-listed biotechs. This barometer includes performance indicators, investor interest and market sentiment gauges of the biotechnology sector and contributes to maintaining the visibility of Euronext listed Biotech companies to investors and the financial ecosystem.

International investors and their interest in Euronext
Since a few years, Euronext has seen a growing participation of US investors. Today, it counts more than 480 declared institutional investors from 30 countries across Europe, the US and Asia investing in its Life Science community. Many businesses have seen the access to international investors as a reason to list on Euronext.

Miguel Payró, CFO of Geneuro explains: “Listing in the US is significantly more onerous in terms of work and costs than listing on Euronext or SIX. For our size at the time of our IPO, Euronext was the best choice given the number of listed biotech SMEs, of biotech investors, brokers and biotech-related events, as well as the strong and supportive EU regulatory framework.”

### Capital raised via IPOs in €m and number of IPOs on Euronext

<table>
<thead>
<tr>
<th>Year</th>
<th>Capital raised via IPO (€m)</th>
<th>Number of IPOs</th>
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<td>2013</td>
<td>90.3</td>
<td>8</td>
</tr>
<tr>
<td>2014</td>
<td>298.4</td>
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</tr>
<tr>
<td>2015</td>
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</tr>
<tr>
<td>2016</td>
<td>137.8</td>
<td>5</td>
</tr>
<tr>
<td>2017</td>
<td>140.3</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>1317.5</td>
<td>49</td>
</tr>
</tbody>
</table>
Join the most vibrant Tech community on European markets

Contact our Local Representatives:

**Germany**

Sebastian Grabert  
Director – Germany Representative  
(Munich)  
+49 160 94 93 15 05  
sgrabert@euronext.com

Michael Schatzschneider  
Director – Germany Representative  
(Frankfurt)  
+49 176 47 87 32 00  
mschatzschneider@euronext.com

**Italy**

Giovanni Vecchio  
Director – Italy Representative  
(Milan)  
+39 335 683 7892  
gvecchio@euronext.com

**Spain**

Susana de Antonio  
Director – Spain Representative  
(Madrid)  
+34 696 37 10 61  
sdeantonio@euronext.com

**Switzerland**

Dr. Søren Bjønness  
Director – Switzerland Representative  
(Zurich)  
+41 763 86 80 07  
sbjpenness@euronext.com

For any other requests please contact Euronext’s ExpertLine:  
MyQuestion@euronext.com

Belgium: +32 2 620 0587  
France: +33 1 8514 8587  
Netherlands: +31 20 721 9587  
Portugal: +351 21 060 8587  
UK: +44 20 7660 8587
Spotlight on Germany
The Biotech Growth Engine

Biotechnology in Germany is a growth engine. In 2016, all key figures such as employees, turnover and R&D expenditure were at an all-time high. The publicly listed companies profit from this positive trend.

Over the past years, the German biotech sector has established as powerhouse in the heart of Europe. This is demonstrated by an annual company survey, which BIOCOM AG conducts annually for more than ten years. Published in May 2017, it reported, that the generated turnover of the German biotech sector for the third year exceeded €3bn. In total, figures increased by 8% to €3.54bn compared to the year before.

Key figures with all-time high
Further upswing has been observed regarding spending on research and development (R&D). For the second time since 2010, the innovation budget cracked the one billion euro mark (+6.3%) and now stands at €1.1bn (2015: €1.04m). With a total of 20,280 (2015: 19,010), there were more employees than ever before working in biotech companies that are occupied wholly or predominantly with modern biotechnological methods. The total number of these companies rose to 615 (2015: 593). Thereby, the following figures and conclusions relate only to the ‘dedicated’ biotechnology companies, as defined by the OECD.

Stable financing situation
The financial investments also improved over the past years. In 2016, around €505m were invested in German biotech companies. A large proportion of the money (€216m) went into the private biotech sector, but the majority of the money (€258m) was invested into the already 22 listed public companies (+5%). In 2016, one German biotech IPO (€31.5m) took place in Frankfurt, the first one since 2007.

Strength in medical biotech
Observers of the German biotech sector will have noted a pretty unchanged picture of the sector when it comes to focal areas: the key task of most biotech companies is developing drugs or new diagnostic methods (see Fig. 16). 306 companies (49.8%) belong to the field of ‘red’ biotechnology – a proportion that has remained steady for many years, but which showed an increase in turnover of 8.1% (€2.5bn), and an augmentation in R&D expenditure of 6.6% (€911m) in 2016.

Growing relevance of diagnostics
A growing part of the biotech sector (91 firms) is dedicated to the development of diagnostics, which reflects the increasing demand for early disease detection, e.g. in the field of infection diseases, and the relevance
of accompanying diagnostics for therapeutic treatments, e.g. for a personalised medicine. This growth is underlined by a large increase of turnover (€1.79bn, +9.3%) and R&D expenditure (€280m, +15.9%), highlighting the importance of these companies for the German biotech sector. Some financings such as the €25m debt financing by listed Curetis N.V. are reflecting this trend.

**Drug developers with full pipeline**
A total of 57 German biotech companies are fully dedicated to drugs and have one or more candidates in clinical development. Last year, a total of 101 biologically active compounds were in one of the three phases (2015: 100). The establishment of a robust clinical pipeline is partly due to the high overall interest in cell therapies and immuno-oncology. Developing pioneering therapies based on the body’s own immune system is the focus of several companies, such as iOmx Therapeutics AG, which develops cancer therapeutics by targeting novel immune checkpoints. Other companies in the field are Immatics, CureVac o BioNTech. Several listed German biotech companies, such as MorphoSys or Medigene, also work in this field.

**MOLOGEN: Pioneer in immunotherapy**
Berlin-based MOLOGEN AG is another example. The company had already recognised the potential of the immune system to fight cancer or other diseases by the 90s – long before immuno-oncology hit headlines across the globe. The company’s lead candidate Lefitolimod is currently tested in a pivotal phase III trial for first-line maintenance treatment of metastatic colorectal cancer and in a phase II trial with lung cancer patients. In addition, a combination study with the checkpoint inhibitor Yervoy® (ipilimumab) is ongoing. “We were among the first to recognize the potential of immuno-oncology therapies and we alone subsequently identified and developed all of our current candidates in the pipeline,” says Mariola Söhngen, CEO of MOLOGEN AG. For more information see company profile page 34.

**Affimed: Harnessing the power of innate and adaptive immunity**
Another immunotherapy specialist in Germany is Affimed. It was founded in...
2000 based on an antibody engineering technology developed by Prof. Melvyn Little’s group at the German Cancer Research Center (DKFZ) in Heidelberg. “Today it’s understood that the development from a healthy cell into a tumour cell is closely related to the immune system and that therapies should activate the body’s own immune cells to destroy the tumour. Back then, it was a novel solution,” explains CFO Florian Fischer who joined Affimed in 2005. The immuno-oncology specialists are among the most advanced in the field working with tetravalent bispecific antibody formats. Moreover, compared to the majority of immuno-oncology companies, Affimed focuses on the power of both T cells and natural killer (NK) cells, aiming to activate adaptive and innate immunity. “We have a particular interest in NK cells as the innate immune system is the first line of defense against malignant cells and our technology has the potential to activate these cells, overcoming tumour immune evasion,” says Fischer. For more information see company profile page 30.

Top 3 financing rounds of listed companies in 2017

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<th>Company</th>
<th>Capital raised</th>
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<tr>
<td>Evotec AG</td>
<td>€90.3m</td>
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<tr>
<td>4SC AG</td>
<td>€40.9m</td>
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<tr>
<td>Heidelberg Pharma AG</td>
<td>€34.4m</td>
</tr>
</tbody>
</table>

Fig. 16: Main areas of activity in German medical biotech companies

© BIOCOM AG
AFFIMED

Seeking to cure patients by harnessing the power of innate and adaptive immunity

Affimed was founded in 2000 based on an antibody engineering technology developed by Prof. Melvyn Little’s group at the German Cancer Research Center (DKFZ) in Heidelberg. In 2007, based on promising preclinical data and also a maturing of the bispecific molecule landscape, the company was able to attract a consortium of high profile US and EU venture capitalist and strategic investors which financed the company through 2014 and invested roughly €90m from this group. “Today it’s understood that the development from a healthy cell into a tumour cell is closely related to the immune system and that therapies should activate the body’s own immune cells to destroy the tumour. Back then, it was a novel solution,” explains CFO Florian Fischer who joined Affimed in 2005, initially on a part time basis.

Today, the immuno-oncology specialists are among the most advanced in the field working with tetravalent bispecific antibody formats. This format allows Affimed’s products to bind both the immune cell and the tumour with high specificity due to two binding sites on each, thereby aiding the immune cell to attack the tumour. Moreover, compared to the majority of immuno-oncology companies, Affimed focuses on the power of both T cells and natural killer (NK) cells, aiming to activate adaptive and innate immunity. “We have a particular interest in NK cells as the innate immune system is the first line of defense against malignant cells and our technology has the potential to activate these cells, overcoming tumour immune evasion,” says Fischer.

Affimed was one of the first European biotech companies that profited from the open IPO window in the US. Since its listing on Nasdaq in 2014, Affimed has managed to raise more than US-$140m. “In Europe, we didn’t think it was possible for us to get our desired amount of money because we were at a very early stage in development in a novel field, that’s why we focused on US investors early on,” explains Florian Fischer.

The Nasdaq proceeds in particular have helped to advance the two clinical projects AFM13 and AFM11. AFM13 has been developed to treat patients with Hodgkin lymphoma and in CD30-positive cutaneous T cell lymphoma. AFM13 is in development both as monotherapy (phase II) and in combination with US-pharma company Merck’s anti-PD-1 antibody Keytruda (phase Ib). AFM11 on the other hand is a T cell engager targeting CD3/CD19. It’s currently in phase I testing to treat non-Hodgkin lymphoma and acute lymphocytic leukaemia. “We are also highly active in our preclinical work, designing and developing the next generation of immune engagers,” Fischer notes.

“A key advantage of being listed on Nasdaq is the access to knowledgeable investors on the US capital markets.”
Affimed N.V., Heidelberg, Germany

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<tr>
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<td>Raised capital via follow-on financings</td>
<td>€75.9m (US-$86.7m)</td>
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<td>Major shareholders</td>
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Interview

Why did you choose Nasdaq to go public in 2014 and was it the right decision?

A lot came together in 2014: at the time, we were looking for larger financing volumes to further develop our early clinical programmes in immunoncology. Simultaneously, there was an open IPO window, a high interest in this topic and other listed peers at the same development stage. This stage was perceived to be too early for an EU listing, so the IPO on Nasdaq was a logical consequence. With our story, we were perfectly suited to fit into this sweet spot. Today, a key advantage of being listed on Nasdaq is the access to knowledgeable investors on the US capital markets. Refinancing options are there at any given time because of the critical mass of biotech specialists.

You have raised more than US-$140m on Nasdaq. What makes Affimed attractive to US investors?

With an approach that focuses on tetravalent bispecific antibodies engaging immune cells, we are top of the league in a highly competitive environment. With our competence in NK cell engagers in addition to the more common T cell approach and our unique technology platform, we’re not doing the same as ten other companies. What makes us additionally attractive to in-

Florian Fischer joined Affimed in 2005 as CFO on a part-time basis. Since September 2014, Dr Fischer is fulltime employed by Affimed. He has a strong track record in various biotech and medtech executive positions.

Dr Fischer is founder of MedVenture Partners - a corporate finance and strategy advisory company focusing on the life sciences and healthcare industry. He was CFO of Activaero GmbH (from 2002 until 2011) and served as CFO of Vivendy Ltd. (2008 until 2013) and as managing director of AbCheck in 2009. Prior to founding MedVenture Partners, Fischer worked with KPMG for more than six years and for Deutsche Bank AG. Dr Fischer holds a graduate degree in business administration from Humboldt University, Berlin and a Ph.D. in public health from the University of Bielefeld.
vestors, is the fact that the field we’re in is not just a hype, it has already proven clinical efficacy. Several novel immunotherapeutics have entered the market and there is a growing understanding of the role of immune cells in cancer biology, allowing for rapid progress. Thus, immuno-oncology continues to be an attractive investment opportunity.

**How are you differentiated from your competitors?**

Our technology has many advantages. Firstly, we are the most advanced company in the field working with tetravalent bispecific immune engagers. By doing so, we are following a dual targeting approach to fight cancer cells: we attack each receptor twofold which makes the antibody highly specific and more effective than others. Secondly, we are able to target both T cells and NK cells. We are one of very few companies with an advanced NK cell approach, having specifically selected CD16A, as the key target receptor enabling NK cell activation. Our NK cell engagers are highly promising for both monotherapy and combination strategies. Thirdly, our engineering expertise has helped us to solve some of the technological challenges connected with bispecific antibody formats. This allows us to rationally design and develop molecules in a variety of formats and with profiles tailored specifically to patient’s needs.

Why are Affimed’s NK cell engager programmes a promising approach in cancer therapy and which advantages do they offer?

AFM13 is our most advanced NK cell engager and our trials serve to generate proof of concept and mechanism. We are especially interested in AFM13’s potential in combination therapies which promise to eliminate tumours through multiple mechanisms. We believe that our preclinical NK cell engagers AFM24 and AFM26 are ideally suited to exploit NK cell mediated cytotoxicity in other indications and settings to AFM13. Both candidates are best-in-class NK cell engagers and, like AFM13, target CD16A, a key activating receptor on NK cells. In addition, AFM24 targets EGFR, relevant to solid tumours, while AFM26 binds to BCMA, a validated target in multiple myeloma. Current studies provide further preclinical evidence of favorable safety profiles for both NK cell engagers and also confirmed their ability to potently and effectively lyse tumor cells, even those with very low target expression.

**DOs**

**Differentiated idea:** You need to have a convincing story to tell the investors. Ideally, you are active in an attractive market and you already have clinical programmes with good data.

**Experienced team:** US investors look for serial entrepreneurs. You need to have a track record in the biotech industry and a broad management team with enough professional experience. With a good reputation, you will be able to convince investors.

**Provide regular updates:** You should keep the news flow ongoing with updates of your activities. Your investors will appreciate regular information on your pipeline and products.

**DON’Ts**

**Start late:** An IPO process needs good preparation. The earlier you start talking with investors, analysts and banks, the clearer you will see whether your story is good enough for the stock market.

**Rush:** Not every bank and not every advisor in the US will be the right one to prepare your company for an IPO. Take your time to carefully consider which partner fits your needs best.

**Make yourself scarce:** Don’t underestimate the time you need to establish your company within the financial community in the US. It’s time consuming and you have to follow a consequent approach. In the long-term perspective, European companies should plan to build up at least a core US team with continuous presence overseas.
MOLOGEN

German pioneer in the field of immunotherapy

Berlin-based MOLOGEN AG is a pioneer for many reasons: Firstly, the company had already recognised the potential of the body’s own immune system to fight cancer or other diseases by the 90s – long before immuno-oncology hit headlines across the globe. Secondly, MOLOGEN was one of the first German biotech companies to list on the stock market, taking this brave step shortly after its foundation in 1998. Today, MOLOGEN is a well-established clinical stage biopharmaceutical company. Its lead candidate Lefitolimod is currently tested in a pivotal phase III trial for first-line maintenance treatment of metastatic colorectal cancer and in a phase II trial with lung cancer patients. In addition, a combination study with the checkpoint inhibitor Yervoy® (ipilimumab) is ongoing. “We were among the first to recognise the potential of immuno-oncology therapies and we alone subsequently identified and developed all of our current candidates in the pipeline,” says Mariola Söhngen, CEO of MOLOGEN AG.

This experience has helped the company to reach late stage clinical phases without any partners. “We have succeed in financing our clinical development stages through the capital market,” Söhngen states. Since the IPO in 1998 at the German Stock Exchange in Frankfurt/Main, MOLOGEN has raised a total of €145m in follow-on financing rounds.

The company’s roots date back to the late 90s when molecular biologists working alongside Prof. Burghardt Wittig at the Freie Universität Berlin (Free University of Berlin), Germany, developed promising new DNA technologies and undertook pioneering research with cell-based therapeutic approaches to treat cancer patients. Based on these findings, MOLOGEN was founded and the proprietary dSLIM® technologies (family of TLR9 agonists) were developed. These days, the company is focusing on its lead candidate Lefitolimod (MGN1703) which belongs to the class of immunomodulators that bind to toll-like receptors (TLRs). These receptors serve to identify pathogens such as viruses, bacteria or fungi, and initially activate the innate immune system and also, potentially activate the adaptive immune system to fight these off. “Based on treatments with more than 450 patients so far, the drug has a favourable safety profile and is well tolerated,” says Söhngen. In addition to the oncology field, Lefitolimod is also being tested for the indication HIV. A phase Ib/IIa study began in 2015 and it has already been extended. Key results have been presented in August 2017. In summer 2017, MOLOGEN announced plans to cooperate with Chinese company iPharma Ltd., to develop, produce and distribute Lefitolimod in China. The final licensing agreement is to include an initial payment at signing of €3m and potential milestone payments of a total volume of up to €100m. In addition, MOLOGEN would receive low double digit royalties on sales.

“We were among the first that recognised the potential of immuno-oncology therapies.”
MOLOGEN AG, Berlin, Germany

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<td>Field of activity</td>
<td>Immunotherapies to treat colorectal cancer, lung cancer and HIV that trigger the innate immune system; immunomodulators which bind to toll-like receptors (TLRs)</td>
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<td>Employees (2017)</td>
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<tr>
<td>Raised capital via follow-on financings</td>
<td>€130.5m</td>
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<td>Major shareholders</td>
<td>Global Derivative Trading GmbH (&lt;25%), Deutsche Balaton Aktiengesellschaft (5%), SIGNAL IDUNA Krankenversicherung a.G. (4%), Baloise Holding AG (4%)</td>
</tr>
</tbody>
</table>
Your listing on the German stock exchange in Frankfurt already dates back 20 years. Are you satisfied with being a European listed company?

Yes, the capital markets here in the EU have supported the growth of the company over a long time. Given the further development of the company, we are now also looking into other markets and have just attracted a US investor in our last financing round.

Globally, there are quite a few companies active in the field of immunotherapy. What makes MOLOGEN AG unique?

We have been working in this field since 1998. Based on our experience, we have developed our technologies and identified promising drug targets. All of the candidates in our pipeline are the result of our own R&D activities and we have succeeded thus far in bringing our most advanced project, Lefitolimod, to a clinical stage III trial.

What is the current state of your most advanced candidate Lefitolimod?

The safety profile after more than 450 patients shows that Lefitolimod is a well-tolerated drug. It is well tolerated compared to other immunotherapies. The IMPALA phase III trial is running according to our expectations for patients with metastatic colorectal cancer. Here, we are testing the candidate...
Establish strong and experienced management!

Prepare financial reporting, control systems and compliance systems!

Identify and select strong partners, e.g., legal and financial advisors, investment banks!

Establish and empower investor relations!

Define and communicate convincing equity stories!

Tell uniqueness of the company!

Deliver your goals on time and ensure quality!

Which partners would be most interesting for Lefitolimod?

From our perspective, there are three groups of companies which would profit the most. Firstly, there are big pharma companies which want to close a gap in immunotherapy or strengthen their portfolio with an advanced product. Secondly, our drug could be a fit for companies already working in the immunotherapy field, with checkpoint inhibitors, for example, but which need a complementary candidate to offer combination therapies to differentiate from other checkpoint inhibitors. Thirdly, our product would be interesting for one-product-companies which want to test their therapy in a combination study.

Which mode of action would suit most in combination with Lefitolimod?

The candidate not only works with checkpoint inhibitors, but it may also improve the efficacy of chemotherapeutics, therapeutic cancer vaccination or oncolytic viruses. This is because, unlike many others, our drug works on the proximal part of the immune cascade. Lefitolimod binds to suitable TLR9 receptors within specific immune cells mainly in so-called plasmacytoid dendritic cells which trigger the immune system to fight against cancer cells. For this reason, a combination of our immune surveillance reactivator with a more targeted cancer approach would make perfect sense.

as first-line maintenance. We reached our goal to include 540 patients in mid-May 2017. The analysis of this trial is expected for 2019. The results of our exploratory phase II study IMPULSE recently demonstrated that we are on the right track. They gave us an initial idea of the efficacy of Lefitolimod for some subgroups of lung cancer patients. For many experts, these results were kind of an eye opener because to date there has been almost no therapeutic success for this difficult indication. Our results, however, were considered as a very positive sign for specific subgroups and will help us to define such groups for studies relevant for approval.

What is your next step?

We are currently focusing on out-licensing or partnering for our lead candidate Lefitolimod and on preparing for its possible market approval. We are looking for global and also for regional partners, especially in Europe, North America and East Asia to develop Lefitolimod further. We are particularly interested in finding a financially strong company which could initiate further clinical trials. The first important step will be an agreement with Chinese company IPharma Ltd., to develop, produce and distribute Lefitolimod in China, for which MOLOGEN signed a binding term sheet this summer.

DON'Ts

Don’t oversell equity story!

Don’t plan with a too tight time schedule!

Don’t underestimate costs and resources needed!

Don’t start without a backup or Plan B!
Annex
Overview and Methodology

European biotech companies are listed on various trading centres in Europe and the US. The overview shows the most important European stock exchanges and the Nasdaq with respect to their biotech IPO and financing activity.

The period under review for this report was Q1/2012 until Q4/2017. In the framework of the study, the most important 14 European trading centres were analysed according to the following parameters:

- number of biotech companies
- number of IPOs
- number of follow-on and other financings
- capital raised via IPOs
- capital raised via follow-on and other financings.

These data were recorded for Euronext and Nasdaq OMX as well as the exchanges in London, Zurich, Frankfurt, Oslo and Warsaw. An analysis of Nasdaq US, New York, and its listed European biotech companies (Israeli companies not included) was also included. At the end of Q4/2017, a total of 233 dedicated biotech companies was counted. Whereas the majority of the firms could be assigned to either a European stock market or to Nasdaq US, there is a total of eight companies that are listed on both sides of the Atlantic. For these companies, the respective capital raised was assigned to the exchange where the financing took place, if not otherwise indicated (e.g. the secondary listing on Nasdaq US). All information stems from publicly available data sources and annual reports, unless otherwise indicated. Within the report, biotechnology was defined as “the application of science and technology to living organisms, as well as parts, products and models thereof, to alter living or non-living materials for the production of knowledge, goods and services.” This definition follows the internationally comparable biotechnology framework of the Organisation for Economic Co-operation and Development (OECD).

For an easy-to-use analysis, data relating to cross-border stock exchanges such as Euronext and Nasdaq Nordic have been cumulated according to their main market and growth market segments – Euronext/Alternext and Nasdaq Main/Nasdaq First North respectively. Market capitalisation of all companies was updated 4 October, 2017. The stock market profiles (see next page) show most of the data compiled.

For the time period 2012 to 2014, foreign currencies others, than EUR have been converted to EUR according to the conversion ratio used in the “Comparative Analysis of European Biotech Stock Markets” published by BIOCOM in January 2015. For all 2015, 2016 and 2017 data, the conversion ratio of the respective date was used. For the 2016 turnover of the companies, a mean ratio for the year was used.
### Key facts of European biotech stock market exchanges

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<td>6*</td>
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<td>82.6 (3)</td>
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<td>2013</td>
<td>44.2 (2)</td>
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<td>2014</td>
<td>182.1 (6)</td>
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<td>2016</td>
<td>127.5 (4)</td>
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<td>2017</td>
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**Total**

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<td>85.4 (7)</td>
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<td>2013</td>
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**Total**

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<td>1,673.4 (21)</td>
<td>561.5 (55)</td>
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*number of companies with a secondary listing on US Nasdaq and their financing

**number of companies exclusively listed on Nasdaq and their financing
## Key facts of European biotech stock market exchanges

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<td>66.4 (1)</td>
<td>–</td>
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</tr>
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<td>31.5 (1)</td>
<td>–</td>
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<td>–</td>
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<td>–</td>
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<td>–</td>
<td>43.6 (1)</td>
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<tr>
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<td>31.5 (1)</td>
<td>–</td>
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<td>118.5 (4)</td>
<td>64.6 (6)</td>
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<td>410.0 (9)</td>
<td>310.0 (1)</td>
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<td>9.9 (4)</td>
<td>1.1 (1)</td>
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<td>2014</td>
<td>378.1 (14)</td>
<td>230.8 (1)</td>
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<td>32.6 (7)</td>
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<td>149.0 (13)</td>
<td>–</td>
<td>352.0 (9)</td>
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<td>2.1 (1)</td>
<td>2.2 (2)</td>
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<tr>
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<td>199.1 (16)</td>
<td>–</td>
<td>28.6 (3)</td>
<td>118.3 (9)</td>
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<td>16.8 (3)</td>
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<td>284.0 (22)</td>
<td>–</td>
<td>167.9 (8)</td>
<td>32.3 (3)</td>
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<tr>
<td>Total</td>
<td>1,629.7 (87)</td>
<td>540.8 (2)</td>
<td>771.6 (33)</td>
<td>233.7 (29)</td>
<td>37.1 (14)</td>
<td>49.5 (11)</td>
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6th Analysis of European Biotech Companies on the Stock Markets: US versus Europe

Destination Growth