Study on investment in the Biomedical industry in Catalonia 2018

Achievements and future challenges
Index

1. Introduction
   - pg. 4

2. International biotech overview
   - pg. 6

3. Investment in biomedicine in Catalonia
   - pg. 9

4. Research and development (R&D)
   - pg. 16

5. Achievements and future challenges
   - pg. 21

6. International benchmark
   - pg. 25

7. Biomedical industry trends
   - pg. 29

8. Conclusions
   - pg. 31

9. Acknowledgments
   - pg. 33
Introduction
Introduction

This study is promoted by CataloniaBio & HealthTech, the result of the integration of CataloniaBio and the HealthTech Cluster. The new association represents the sector in a more transversal way, promoting the convergence of biopharma, medical technology and digital health, to bring valuable solutions to healthcare.

The Catalan life sciences and healthcare industry, in which this document focuses, continues to show signs of strength, as its companies increase their ability to attract foreign investment and their pipeline of products progressively advances towards the later phases of R&D. These are two of the main highlights of the II edition of this study on Investment in the biomedical industry in Catalonia, that presents the main investment indicators for 2017. The monitoring of relevant indicators is a key aspect in the evolution of our companies and will contribute to raise awareness on the leading research and the pioneering innovation that is being carried out on drugs and medical technology by the Catalan ecosystem.

The objective of the study is to provide a specific analysis of the investment as a basis for the different agents to identify global and local trends year after year and reflect on the strategic decisions to successfully face future challenges.

The study analyzes a universe of more than 200 companies, the vast majority of them members of CataloniaBio & HealthTech, based in Catalonia, dedicated to product development (biotechnology, diagnosis, medical devices, etc.), scientific and non-scientific services, pharmaceutical groups and specialized investment entities, and has been complemented with information obtained from public databases.

You can send us comments and suggestions to secretaria@cataloniabioht.org.
International biotech overview

Globally, the biotech industry is returning to stability after years of exponential growth. Total industry financing increased by 12% in 2017, with substantial differences between the US (+42%) and Europe (-51%). After a weak start, the second half of the year reported more robust follow-on offerings and initial public offerings (IPOs) and the environment for early stage ventures became more plentiful. A solid pipeline of privately held biotechs backed by a combination of traditional and strategic investors kept the market awake.

Contrary to the evolution of M&A, the biopharma strategic alliance landscape has kept stable. The amount of collaborations has risen by 2% in 2017, in line with the overall spending allocated to these operations.

In terms of global R&D spending, 2017 has set a new record. There is a steep and deep pipeline of new innovations emerging, with both big pharmas and small startups opening new horizons with unprecedented mechanisms and novel medicines. However, backlash in government and public circles to biopharmaceutical pricing and the prioritization to review generics and biosimilars’ applications may pose some threats to achieve new highs in R&D investment in 2018.

In 2017, some of the global volatility present in 2016 lessened and that was apparent in the rebound of the aggregate biotech market capitalization, which rose 23% globally. However, sky-high valuations, free-flowing cash for startups, and uncertainty about tax reforms led to stagnation in mergers and acquisitions (M&A). The total volume and value of life sciences industry M&A fell nearly 20% last year. Bucking these trends, Medtech M&A value rose 50%, driven by companies seeking economies of scale in the face of increasing leverage from payers.

Much of 2017’s M&A was fostered by three strategic drivers: the need for inorganic growth to fill revenue shortfalls, the pursuit of economies of scale in the face of increasingly consolidated customers, and strategies to access complementary product lines or new geographic territories. Agreements illustrate the demand for products and pipeline in growth areas like specialty therapies and oncology.

In 2013, the biotech industry was characterized by four main categories of funding: venture, debt, follow-on & other, and IPO. In 2017, the industry has seen an increase in venture capital and debt financing, with a decrease in follow-on & other and IPO funding.
In terms of financing, early 2018 operations anticipate a strong private financing climate fueled by the breathtaking pace of innovation and well-funded venture capital firms. Corporate investors eager to participate in early stage innovation, public market investors seeking to get in before an IPO, and unconventional investors keen to put long-term capital to work behind innovation are also augmenting the pool of financing opportunities.

In M&A, more deal making is likely in 2018 as the collective firepower in biopharma and Medtech sectors surges and larger companies see an increasingly crowded field of smaller, high-growth competitors. Well-capitalized non-traditional buyers, whether they are technology giants or new health care or financial entrants, are also interested in the same M&A opportunities.
Investment in biomedicine in Catalonia
Investment in biomedicine in Catalonia

Number of operations and capital raised in 2017

102 M€
raised

30 operations

Financing sources for the operations in 2017

In 2017, 102 million euro were raised, being 3.4 million the average size per operation.

In 2017, 30 financing operations were carried out in Catalonia, through which the sector raised 102 million euro.

The largest investments (>15 million euro) accounted for 10% of the total, while 52% of the operations exceeded 2 million euro.

Venture capital firms are the main investor (33%) in product development companies. They also rely on public debt (18%) and institutional investors (15%), which have been the source of funding in the largest operations of the year. Additionally, industrial partners and the public market (MAB) have contributed with 14% of the total capital raised. Service companies were mainly financed through private debt (74%), followed by entrepreneurs (14%), family, fools and friends (7%) and industrial partners (6%). Private debt has also been the main financing source for pharmaceutical companies.

There are significant variations in the financial strategy followed by companies from different typologies.
Founders finish the first round with the 88% of the total participation and, at the end of the third round, they still control, on average, 49% of the company.

Business angels and family offices are a recurrent financial partner for product development companies. They own 6% after the first round to end up owning 25% of the shares after the third one.

Other agents with relevant participation are venture capital firms, which rise their share from 2% after the first round to 19% in the third one.

Investors based in Catalonia account for 76% of the capital share, while international investors and those coming from the rest of Spain own 16% and 8% respectively.
### Operations of Catalan investment companies in 2017

**31 operations**

<table>
<thead>
<tr>
<th>Capital committed (M€)</th>
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<tbody>
<tr>
<td>2016</td>
<td>31.9</td>
</tr>
<tr>
<td>2017</td>
<td>55.7</td>
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<tr>
<td>% Total</td>
<td>48%</td>
</tr>
<tr>
<td>% Catalonia</td>
<td>33%</td>
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<tr>
<td>+74%</td>
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<table>
<thead>
<tr>
<th>Capital disbursed (M€)</th>
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<tbody>
<tr>
<td>2016</td>
<td>25.7</td>
</tr>
<tr>
<td>2017</td>
<td>47.1</td>
</tr>
<tr>
<td>% Total</td>
<td>57%</td>
</tr>
<tr>
<td>% Catalonia</td>
<td>29%</td>
</tr>
<tr>
<td>+84%</td>
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- **31 operations**
  - **Capital committed (M€)**: 31.9 (2016) → 55.7 (2017) (+74%)
  - **Capital disbursed (M€)**: 25.7 (2016) → 47.1 (2017) (+84%)

### Time operating with the available cash without the need for new financing in product development companies

- **41%** of the companies will have to resort to new financing sources in less than one year.

#### Around 41% of the companies will have to resort to new financing sources in less than one year

41% of the product development companies estimate that the time of survival with the available resources is less than one year, having revenues in 33% of the cases. On the other hand, 25% state that it will not be necessary to carry out more operations in a period of more than two years, as 86% of them already have revenues that ensure their sustainability. The other 34% expect to be able to wait between one and two years, with 50% of them having revenues.
In 2017, a total of 31 investments were performed by investment companies based in Catalonia. Financial resources committed amounted to 56 million euro, of which 33% was allocated to financing rounds carried out by Catalan companies. The value of these operations rose by 74%, meaning that the average value per transaction has rocketed in 2017.

Investment rounds in Drug discovery companies continue to be the most common (71%), while Medtech accounts for the remaining 29%.

There is a real balance when comparing recurrent versus new investment operations. Half of the operations were started from scratch in 2017, while the remaining transactions were follow-ons. This fact indicates that companies are being able to maintain investors’ confidence.

Venture capital firms emphasize that 2017 has left positive results and several improvements that go beyond the total investment figure. Investors affirm that three major trends have been consolidated:

1. **Larger investment rounds:** Investors are now less keen on fractional investments. Therefore, the capital to be raised is accumulated in less but larger rounds in terms of value.

2. **Increasing participation of international funds:** The volume of foreign investment made in Catalonia has risen in 2017 and more international venture capital funds are looking to invest in the region. Their contribution is expected to be key in the near future, since there is currently a significant number of companies expected to open late stage funding rounds of considerable size which cannot be covered by local investors. In this context, the ecosystem will need to reinforce its international visibility in order to strengthen its financial muscles.

3. **Evolution of management teams:** Among early stage companies (seed capital rounds), the quality of CEOs is perceived to be improving and becoming more and more prepared, flexible and receptive to changes. However, experts state that in more advanced stages (round A), there is still room for improvement in terms of the expectations of quality, credibility and expertise levels that investors are looking for in company CEOs. In addition, investors are increasingly analyzing the capabilities of other team members such as the scientific director and the medical director, who are deemed to be key for a robust design and implementation of clinical studies.

Venture capital experts agree that the total financing raised in 2016 by the Catalan biomed sector was a too large quantum leap considering the preceding years, and that this level of growth cannot be expected every year. Most of them consider that 2017 has fulfilled the expectations and that the current political conjunction had no significant impact on investments. Moreover, they stress the importance of the deal undergone by Stat Diagnostica as a very significant milestone for the industry, since the company has completed the whole process (from startup launch to the point of being sold to a large corporate player in the pharmaceutical industry).

In view of the start of 2018, there is broad consensus that this year will resemble 2017. Venture capital firms expect more exits, either through sales or IPOs. In addition, some of them are reloading their funds, which means that their space will need to be covered by other agents such as business angels.

In order for Biotech and Medtech companies to be successful, Catalan leading venture capital firms recommend to master the following topics:

- Strengthen management teams
- Leverage on second generation entrepreneurs who can act as catalysts, helping newly created projects
- Devise a financing strategy that aligns with prevailing market dynamics
- Communicate a clear relationship between time, capital requirement and milestones, and ensure a financing strategy toward an exit milestone and clear path to liquidity
### Destination of R&D investment in 2017

More than 3 out of 4 of the R&D economic resources were allocated to Catalonia.

Most of the R&D projects (76%) were devoted to companies allocated in Catalonia in 2017. The European market gains weight receiving 11% of the funds (6% in 2016), while the 11% and 2% allocated to national and international agents remain stable.

### Licensing agreements and their potential value in Catalonia in 2017

Companies expect to obtain 13M€ by licensing their products.

A total of 32 licensing agreements were signed in 2017, coming the majority of them from product development companies. Through these licensing agreements, companies expect to generate potential revenues of 12.6 million euro in the near future.
Pharmaceutical companies with stakes in biotechnology companies in 2017

55% of the pharmaceutical companies are committed to investing in and participating in biotech companies.

Of the invested companies, 80% are based in Catalonia and in the international market, divided in equal parts. The remaining 20% of the investees are located in the rest of Spain.
4 Research and development (R&D)
Biopharma companies have experienced great progress in their pipeline in 2017. In 2016, 72% of the projects were in the preclinical validation phase, while in 2017 this percentage has been diminished to 51% (32% preclinical non-regulatory validation phase and 19% preclinical regulatory validation). With regards to late stage projects, 7% of them are now in the approval phase, close to market launch.

Similarly to biopharmas, Medtech companies have been able to reduce the percentage of projects in early stages (product development and prototyping) from 66% in 2016 to 46% in 2017. These companies have 19% of their projects already in the market.
The last stages of development concentrate 26% of the projects. Among these final stages, projects in phase IV, which is becoming increasingly relevant for market access, are the most numerous (15% of the total).

Pharmaceutical companies also have a very dynamic phase III activity, which accounts for 32% of the projects.

Discovery and preclinical validation stages concentrate a lower percentage of projects compared to the previous year.
Companies in the sector focus their innovation on oncology (30%), central nervous system (16%), infectious diseases (15%), cardiovascular system (12%) and respiratory system (12%).

Oncology is still the first and main therapeutic area, repeating the result obtained in 2016.
The collaborative projects have been distributed in a balanced manner among the different potential partners. Research centers have been the choice in 29% of the projects, while academic centers and start-ups concentrate 27% of the projects each.

There has been a significant increase in the number of collaborative projects with start-ups, especially among pharma companies (57% of their projects), showing the increased willingness to partner with other members of the ecosystem in order to innovate. Product development companies usually collaborate with research centers (43% of their collaborations) and service companies prefer to join efforts with academic centers (31% of their collaborations).
Achievements and future challenges
Investment in biomedicine in Catalonia

Key milestones achieved by Catalan companies in 2017

In the case of product development companies, reaching agreements with strategic partners and raising financing have been the most important accomplished objectives. Demonstrating the economic value of innovation has also emerged as a new achieved milestone by some of the companies surveyed.

The main objectives achieved by service companies have been the expansion of the portfolio and the increase in customers and turnover.

Finally, pharmaceutical companies have managed to overcome administrative and/or regulatory barriers, which gain importance when approaching the final stages of the R&D process and market access needs to be planned. In this phase, demonstrating the economic value of the innovation is critical.
Achievement of objectives in 2017

Half of the companies consider they have partially or totally fulfilled their objectives.

Approximately 50% of the companies have met or exceeded the objectives set at the beginning of 2017. Only 7% of product development and service companies were not able to accomplish them.

Risks to the viability of companies

Companies consider financial risks to be the most critical.

When selecting the risk that concerns them the most, 62% of the companies refer to financial risks. Scientific risks are perceived as the second most relevant hazard (25%), far from management risks (9%).
Main challenges for the year 2018

- Raise financing
- Reach agreements with strategic partners
- Demonstrate the economic value of innovation
- Administrative and/or regulatory barriers
- Get to the market
- Complete a clinical phase
- Maximize the efficiency
- Transform products into services
- Other

The main future challenge of biomedical companies continues to be raising funds

The greatest future challenges for the companies in the bioregion are, in this order, raising financing and reaching agreements with strategic partners. They are followed closely by market access demands such as demonstrating the economic value of innovation, overcoming administrative and regulatory barriers, and getting to market.

Most ranking positions remain unchanged when comparing the results of 2017 with the ones of 2016, with the exception of reaching the market and administrative and regulatory barriers which have swapped positions.

Companies looking for a partner for the development or commercialization of their innovations

57% of the companies are looking for a partner

- 26% R&D
- 44% Commercialization
- 30% Both
- 25% Both Commercialization
- 25% Commercialization
- 75% R&D

6 out of 10 companies are actively looking for partners for development and/or commercialization

57% of the companies affirm they are seeking to reach agreements with partners for development and/or commercialization of their products.

In line with the nature of their activities, pharmaceutical (100%) and product development companies (74%) are the most active in looking for this kind of agreements.
6 International benchmark
International benchmark

Main figures in terms of funds raised, number of companies and people employed

The concept of cluster-based organization has become increasingly relevant in the Life Sciences industry. Through their implementation, cluster constituents enjoy the economic benefits of several positive location-specific externalities and reap their full potential. Access to specialized human resources, knowledge spillovers, pressure for higher performance in head-to-head competition, and learnings from the close interaction with specialized customers and suppliers are some of these externalities.

Successful regions in generating proper business environment conditions such as Toronto (Canada), Munich (Germany), Greater Copenhagen (Denmark and Sweden) and Israel have been assessed hereafter to gain knowledge about the best practices in the international space.

Except for CataloniaBio & HealthTech, the amount of capital raised accounts for the entire country.
BioM is a network organization of the biotechnology sector in Munich and Bavaria (Germany), formed mainly by product development companies (62%); service and pharmaceutical companies represent 26% and 12% respectively.

In the last years, its revenue growth has been sustained in 5.5%. The decrease in the investment of venture capital companies is being offset by the increase of business angels, among which individual investors that bring very significant amounts of funding to the table can be found.

Currently, its main objective is to foster digitalization and fuel the cardiovascular field.

Medicon Valley Alliance is a non-profit membership organization in the Danish-Swedish life science environment, based in the Greater Copenhagen region. It is mainly composed by product development companies (81% of the total) with a clear focus on Medtech.

Capital inflows from the United States, China, Germany and the United Kingdom are essential to keep the dynamism in the area. Regenerative medicine and cell therapies have the backing of investors.

There is high commitment from companies to bet for digital health. The government has recently created national committees to promote the sector.
To Health! is an industry-led promotion cooperative located in Toronto (Canada). It has been growing at a quicker pace than other international clusters due to the investment of large multinationals such as Bayer, Versant Ventures, Johnson & Johnson, Celgene and General Electric.

The cluster is a global reference in regenerative medicine and stem cell research, leading research and product development in this area. One of its main objectives is to increase corporate investment.

Israel Advanced Technology Industries (IATI) is based in Tel Aviv (Israel). The ecosystem swivels around technology, and the weight of medical device companies (40%) overtakes that of biotech firms.

In Israel, there is a great participation of the public sector in the promotion and financing of companies, but the cluster leaders expect a greater participation of the private sector in years to come. Plans are underway to boost the investment of local venture capital firms, since they only represent 13% of the total capital invested.
Biomedical industry trends
Biomedical industry trends

The ever-changing Life Sciences industry requires biotech management teams to stay nimble and be able to navigate multiple trends and uncertainties. Demonstrating value, increasing R&D efficiency, embedding digital capabilities, anticipating regulations and adapting the organizational structure to market needs are vital topics in managers’ agendas in 2018.

Ongoing pricing pressures force companies to emphasize value demonstration. Investing in real-world evidence to capture patient-centric data, using biomarkers to segment populations, incorporating stakeholders’ definition of value as early as possible, and being proactive in the design of outcome-based contracts and around-the-product services are some of the vehicles being used to demonstrate value and meet payers’ requirements.

As prices decline and margins erode, improving R&D efficiency gains relevance. With this aim, companies are adopting new solutions such as precision medicine (delivering the right drug to the right patient at the right time through the use of biomarkers), adaptive trials (preplanned alterations in clinical trials through statistical methods), and risk-based monitoring (predictive analytics to manage trials from recruitment to data capture) in order to shorten development time and increase the flexibility and the probability of success.

It is clear that the biotech space is moving from clinical science supported by data to a data-driven science supported by clinicians. Digital entrants are encroaching and building platforms of care, therefore partnerships are essential to access new digital capabilities and master fields such as artificial intelligence, predictive analytics and the internet of things which will be present along the value chain.

The technological transformation has also led to updates in regulation, bringing further challenges for the Life Sciences industry. In 2017, new regulations for medical devices (MDR and IVDR) were released at a European level, and the General Data Protection Regulation (GDPR) has just come into effect in May 2018. Being aware of the new set of rules relating to the collection, storage and processing of personal data will be crucial to avoid data breaches that could result in significant legal and financial consequences.

All in all, in the coming years the life sciences industry will require creative strategies for growth, alternative business models, new paths to innovation, greater efficiencies and additional skills. Embracing flexible organizational structures and cross-functional teams will be key to succeed.
Conclusions
Conclusions

The Catalan life sciences and healthcare sector continues to show solid figures, with 102 million euro in financing secured by biomedical private companies in 2017, according to this second edition of our Study on investment in the Biomedical industry in Catalonia. Product development companies have an increasingly diverse number of financing sources, being venture capital the most common one (33% of all financing raised by product development companies in 2017), followed by public debt and institutional investors; while service companies are essentially financed through their own commercial activity and private debt.

There is a growing interest of foreign investment funds in the Catalan market, with up to 16% of the shares of biomedical companies owned by foreign investors. Biomedical investment companies based in Catalonia also showed strong fundamentals, committing a total of 55.7 million euro in 2017, of which 33%, was allocated to investments carried out in Catalonia. In addition, these companies have already disbursed 47.1 million committed in 2017 or in previous years. 71% of the operations involved drug discovery companies.

Compared to the previous year, the value of transactions led by investors based in Catalonia rose by 74%, meaning that the value per operation has rocketed. All, in a year in which the sector has seen significant milestones that constitute proof of its progressive consolidation.

Biopharma companies’ pipelines are evolving into more advanced R&D stages, with 51% of projects in preclinical validation phases and 7% in approval phase and therefore, very close to market launch. In the case of Medtech companies, 19% of their R&D projects have already reached the market. Oncology, central nervous system, infectious diseases and cardiovascular system are the main therapeutic areas in which Catalan biomedical companies are concentrating their R&D resources, in line with global trends.

In a global context in which silos are being broken and the life sciences and healthcare industry is facing major competition by new players entering the market, it is increasingly critical that companies look to collaborate with other players within their ecosystem in order to boost innovation. Last year, 146 collaborative projects were signed between product development, service and pharma companies, research and academic centers, start-ups and other agents in Catalonia. There is a significant increase in the number of collaborative projects with start-ups, especially among pharmaceutical companies.

The close relationship between researchers, academia, hospitals and companies represents one of the biggest strengths of the ecosystem. Still, there is the goal to enhance the linkages between businesses, universities and public administrations.

Looking to the future, raising financing continues to be the main concern for the companies in the sector, with 62% of the entities surveyed in this study identifying financial risks as the main challenge for their survival in the future. However, as R&D pipelines move closer to market stages, new concerns arise, such as the need to reach strategic agreements with partners, demonstrate the economic value of innovations and overcome administrative and regulatory barriers.
Acknowledgments
Acknowledgments

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We also want to mention the involvement and support of Biocat in the preparation of this study in order to ensure an accurate picture of the sector.
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