## BIOTECH IN LATIN AMERICA

The next frontier

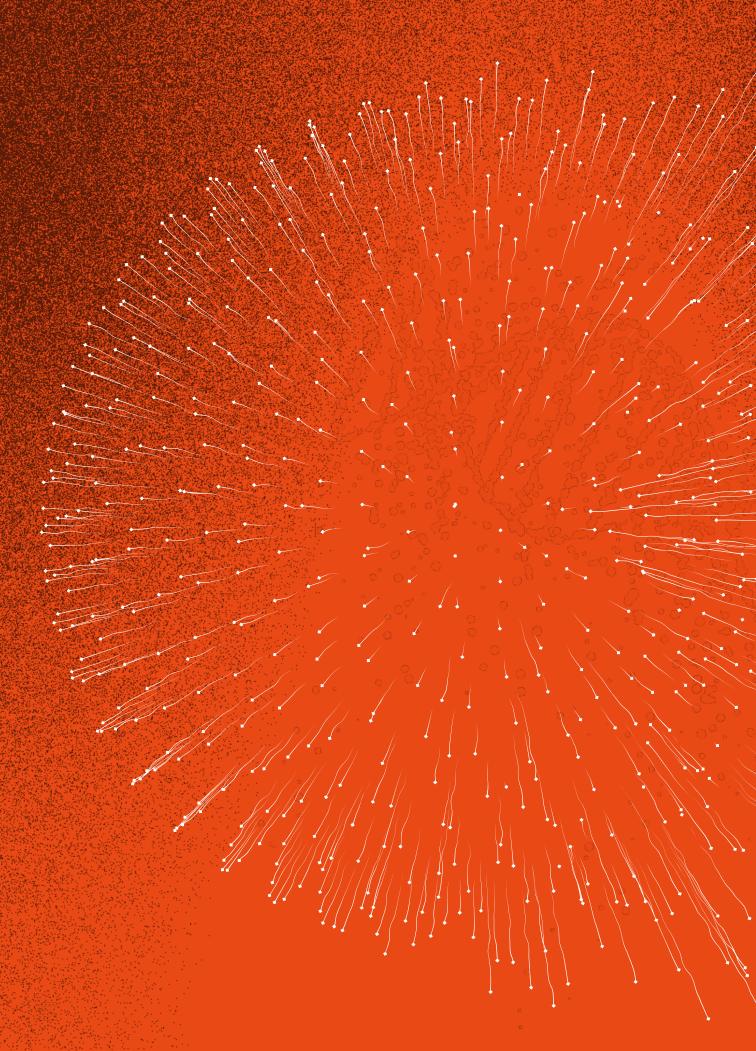




#### Zentynel Frontier Investements is setting up a US \$ 60 million fund to support with financing and specialized management skills the development of biotechnology ventures focused mainly on Latin America.

The main objective of this document is to present the opportunity to develop a VC fund specialized in Biotechnology with a focus on Latin America.

1_	Opportunity to invest in a Biotech Ventu	ure Capital	
	focused on Latin America	G	)5
2_	Venture Capital Biotechnological funds	in Latin America-	13
3_	Biotechnology		9
4_	The Biotechnology Industry	2	29
5_	Zentynel VC		35
		一、人口、人口、人口、人口、人口、人口、人口、人口、人口、人口、人口、人口、人口、	1.5



### OPPORTUNITY TO INVEST IN A BIOTECH VENTURE CAPITAL FOCUSED ON LATIN AMERICA

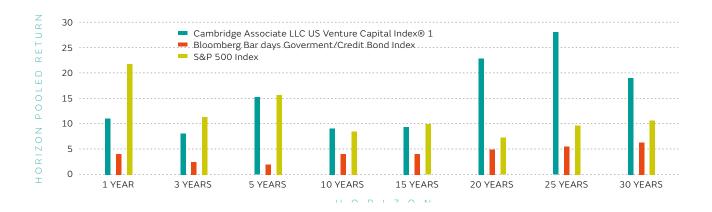


#### **1.1\_** HISTORICAL RETURNS OF VENTURE CAPITAL IN THE USA

 The Cambridge Associates LLC US Venture Capital Index® is a horizon calculation based on data compiled from 1,794 US venture capital funds (1,150 early stage, 210 late & expansion stage, and 434 multi-stage funds), including fully liquidated partnerships, formed between 1981 and 2017. Sources: Cambridge Associates LLC, Bloomberg Barclays, Dow Jones Indexes, Frank Russell Company, Standard & Poor's, Thomson Reuters Datastream, and Wilshire Associates, Inc. Venture Capital is an asset class that provides higher returns to other asset classes over long periods of time than bonds and indexes. This is especially evident in the return obtained by the top quartile of managers who consistently show outstanding performance.

Based on the Cambridge Associates LLC US Venture Capital Index<sup>1</sup>, an index that groups the performance of more than 1,750 funds of all sizes and investment strategies between 1981 and 2017, it is possible to compare the performance of this asset class (net return on Limited Partners) versus the performance of the S&P index and government bonds. The following chart presents a comparison of the annualized returns for each asset class for different investment horizons:

#### US VENTURE CAPITAL: Fund Index Summary: Horizon Pooled Return Net to Limited Partners



- (2) It refers to a higher valuation of a company in future rounds, but it doesn't imply a cash out for the investor.
- (3) The Invesco White Paper Series, The case for Venture Capital: Figure 2: Modest correlation with other asset classes:
  Cambridge Associates Global Venture
  Capital, Global Private Equity, and Global Real Estate Benchmarks Return Report.
  Venture capital, private equity and real estate data from Cambridge Associates.
  Returns for period dating 1990-2014, as of Dec. 31, 2015.

Venture Capital shows a significantly higher performance in horizons greater than 20 years. On the other hand, during the last decades, VC's performance have been similar to that of the S&P and far superior to that of bonds throughout the period. It is important to mention that the returns of recent years of VC are not usually a complete reflection since an important part is in "unrealized gains<sup>2</sup>".

Additionally, Venture Capital can generate higher returns over horizons greater than 20 years<sup>3</sup> than assets such as stocks and bonds.

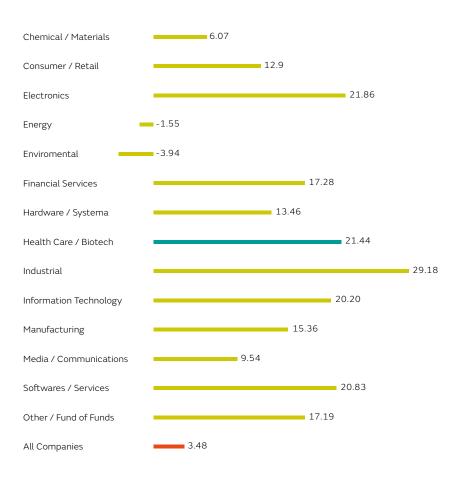
This effect is reinforced in situations such as the current crisis generated by COVID-19, in which a series of techn and biotechn assets have shown significant appreciations (e.g. due to the acceleration in the adoption of certain technologies, or the need for virus diagnosis) versus the adverse impact it has generated in practically all industries.

#### **1.2\_** HISTORICAL RETURNS OF BIOTECH VENTURE CAPITAL IN THE USA

The Venture Capital funds related to Biotechnology have generally shown a performance superior to the average of the Venture Capital funds, and in general superior to any other specific segment except Industrial. The Biotechnology funds have shown average returns for Limited Partners, net of commissions, above 21% per year between 2000 and 2017, as shown in the following table<sup>4</sup>:

#### US Venture Capital:

Average Pooled Gross IRR (%) of Companies Receiving Initial Investment In



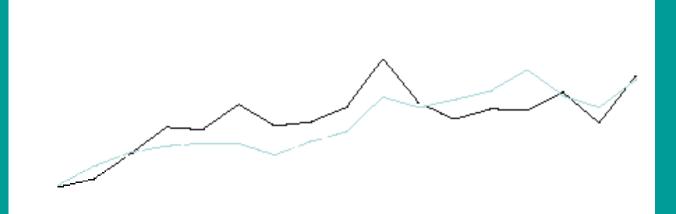
It is interesting to note that, on one hand, Biotechnology funds have consistently shown attractive returns with less volatility than other segments (e.g. lower effects from the dotcom bubble burst), and additionally they have been increasing their performance in recent years, showing exceptional annual returns in the period between 2011 and 2015.

Both phenomena can be observed in the following tables:

(4) Source: Cambridge Associate LLC US Ventures Capital Index

<b>US Venture Capital:</b> Average Pooled Gross IRR (%) of Companies Receiving Initial Investments In	Althrest 200 to 2016	Attratical ease of to 2015	Althreat 200 to 2010	Arthetical as 2015
Chemical / Materials	6.07	-19.71	-4.38	45.51
Consumer / Retail	12.9	<b>7</b> .512.9	2.99	27.63
Electronics	21.86	-2.11	3.75	66.26
Energy	-1.55	1.55	-4.96	-2.61
Enviromental	-3.94	-63.99	-26.53	21.23
Financial Services	17.28	19.51	7.94	21.32
Hardware / Systems	13.46	-0.78	25.88	24.00
Heath Care / Biotech	21.44	9.88	15.62	40.84
Industrial	29.18	36.97	1.51	40.50
Information Technology	20.20	<b>—</b> 13.5	25.57	23.18
Manufacture	15.36	2.32	14.32	31.94
Media / Communications	9.54	4.04	10.98	16.26
Softwares / Services	20.83	10.98	23.68	29.64
Other / Fund of Funds	17.19	6.16	13.59	32.23
All Companies	<b>—</b> 3.48	-2.75	■ 4.24	8.96

US Venture Capital: Since Inception IRR by Company Initial Investment Year By Industry

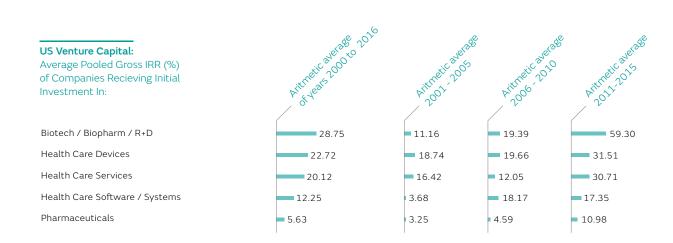


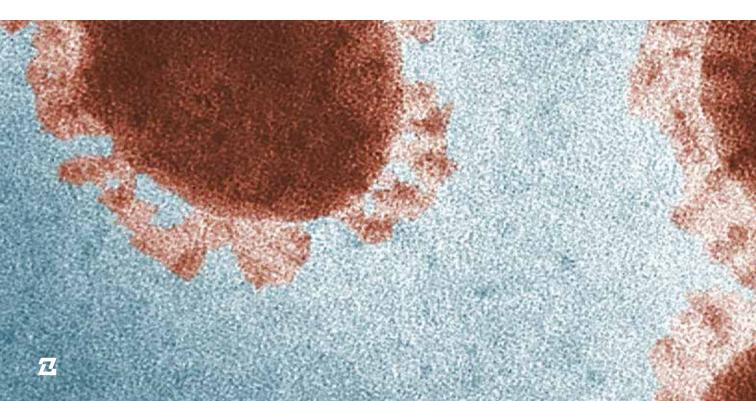
zentynel

#### **1.3\_** HISTORICAL RETURNS OF BIOTECHNOLOGICAL COMPANIES THAT RECEIEVED INVESTMENT FROM VENTURE CAPITAL IN THE USA

There is a great dispersion in the returns of the different investment subgroups of Biotech and Healthcare areas.

When the returns (IRR (%)) of the companies that received VC investments in the respective years between 2000 and 2016 are analyzed, it is possible to conclude that the areas that show the highest returns are those related to Biotech/Biopharma/R&D with an annual average of 28.75%, followed by Pharmaceuticals with an annual average of 22.72% and then Health Services (Healthcare) with 20.12% and medical software systems, medical devices that show an average annual average of 5.63%, with an annual profitability of 12.25% (note that this is the profitability of companies at the level of VC funds).

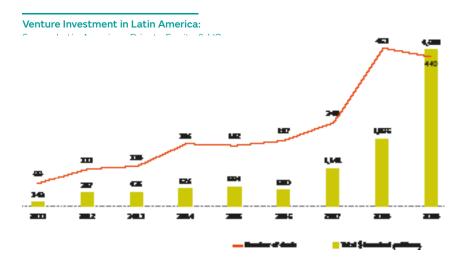




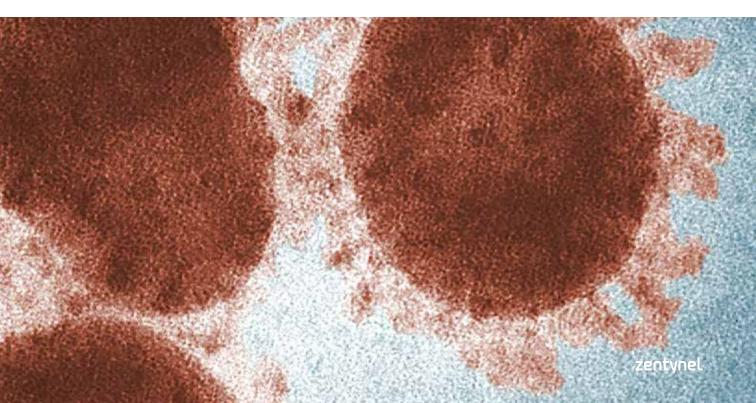
#### **1.4\_** EVOLUTION OF VENTURE CAPITAL IN LATIN AMERICA

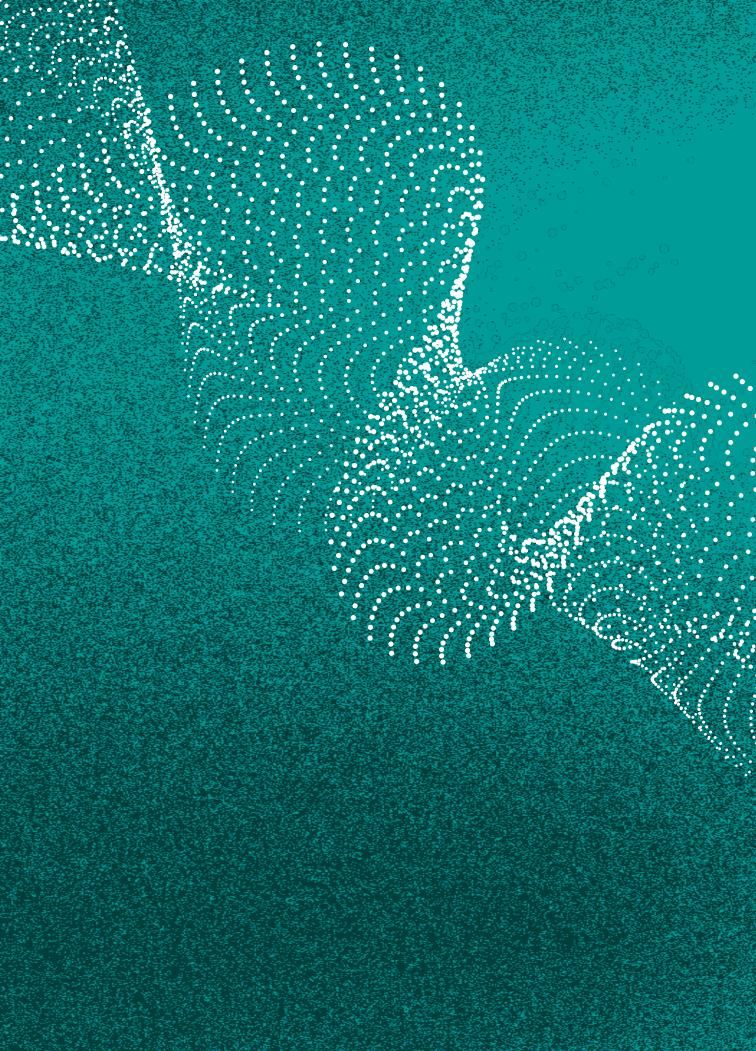
(5) Source LAVCA: https://lavca.org/industrydata/inside-the-4th-consecutive-peak-yearlavcas-annual-review-of-tech-investmentin-latam/

Venture Capital has been growing consistently in Latin America. In the last year (2019) the amounts doubled compared to 2018, reaching a record of US \$ 4.6 billion in 440 operations.



This growth has been accompanied by an increase in joint ventures between local investors together with global players, reaching 37% of invested capital<sup>5</sup>. Furthermore, at least 70% of the investments were made as joint ventures between 2 or more investors.





### 2 | BIOTECH VENTURE CAPITAL FUNDS IN LATIN AMERICA

#### **2.1\_** FUNDS BY COUNTRY IN LATIN AMERICA

The region is dominated by funds oriented to B2C services with a focus on information and communications technologies such as fintech, social media and e-commerce, and in the B2B area with a focus on corporate logistics and Software.

To date, we have identified a total of 156 funds of different sizes operating in Latin America. This includes funds that, although operational, are in the divestment stages and are not adding new companies to their portfolio.

#### 2.2\_

#### MAIN ACTIVE STAKEHOLDERS OF VENTURE CAPITAL IN LATIN AMERICA

Currently the main VC players, according to the investment stage are:

INVESTMENT STAGE	FUND	COUNTRY
Seed Stage	• Canary	• Brazil
-	<ul> <li>Bossa Nova Investimentos</li> </ul>	<ul> <li>Brazil</li> </ul>
	<ul> <li>MAYA Capital</li> </ul>	<ul> <li>Brazil</li> </ul>
	<ul> <li>Monashees</li> </ul>	<ul> <li>Brazil</li> </ul>
	<ul> <li>Global Founders Capital</li> </ul>	• USA
	<ul> <li>Y Combinator (aceleradora)</li> </ul>	• USA
	<ul> <li>500 Startups (aceleradora)</li> </ul>	• USA y MX
Later Seed	KaszeK Ventures	Argentina
and Series A	<ul> <li>Canary</li> </ul>	• Brazil
	<ul> <li>Bossa Nova Investimentos</li> </ul>	<ul> <li>Brazil</li> </ul>
	<ul> <li>Crescera Investimentos</li> </ul>	<ul> <li>Brazil</li> </ul>
	<ul> <li>Monashees</li> </ul>	<ul> <li>Brazil</li> </ul>
	• IGNIA	<ul> <li>Mexico</li> </ul>
	<ul> <li>DILA Capital</li> </ul>	<ul> <li>Mexico</li> </ul>
	<ul> <li>Allvp</li> </ul>	<ul> <li>Mexico</li> </ul>
	Redpoint Ventures	• USA
	QED Investors	• USA
	<ul> <li>SoftBank Latam Fund</li> </ul>	• Latam
Series B and C	<ul> <li>KaszeK Ventures</li> </ul>	<ul> <li>Argentina</li> </ul>
	<ul> <li>Valor Capital</li> </ul>	• Brazil
	Atlantico	<ul> <li>Brazil</li> </ul>
	<ul> <li>Redpoint Ventures</li> </ul>	• USA
	<ul> <li>Riverwood Capital</li> </ul>	• USA
	General Atlantic	• USA

#### 2

- (7) Based on Lavca's record, so it it possible there are more transactions not registered by Lavca.
- (8) https://www.businesswire.com/news/ home/20200909005240/en/NotCo-Closes-85-Million-Series-Announces-Expansion
- (9) https://agfundernews.com/amazon-forag-agrofy-closes-23m-series-b-in-latamslargest-ever-agtech-deal.html

It is important to note that a large part of these players are multi-focal funds while others have focused on IT

At a global level, but not in Latin America, biotechn investment in more advanced stages - series A rounds to series D rounds - is usually led by specialized funds with in-depth knowledge of science and technologies in the Life Sciences area.

#### **2.3\_** FUNDS BY COUNTRY IN LATIN AMERICA

To describe the relevant players in Latin America, it is best to focus on the operations that have occurred in the industry:

Last year was one of the most active in terms of investments in Biotechnology and Digital Health, reaching a total of 32<sup>7</sup> transactions (52% more than 2018) mainly centered in seed / incubation rounds and early stage rounds, being only surpassed by fintech (the leading industry by excellence). Additionally, Biotechnology applied in Agriculture concentrated another 2% of the number of transactions, also centered in early rounds, and Biotechnology applied in food has also been an area that has shown an increase in transactions in Latin America.

Here is a summary of the most relevant transactions:

- Notco<sup>8</sup> (Round for US \$ 85M with participation of L Catterton, Future Positive, Humboldt Capital, The Craftory, Bezos Expeditions, Maya Capital, Kaszek Ventures).
- Agrofiy<sup>9</sup> (Round for US \$ 23M with participation of SP Ventures, Fall Line Capital, ACRE Capital)

It is also worth mentioning smaller deals such as Levita Magnetics, Labi Exames, SouSmile and more than 25 Latin American companies invested in the seed stage.

On the other hand, it is also important to highlight the interest of international Biotech VC Funds willing to participate and co-invest mainly in more advanced stages (rounds greater than US \$ 10 MM) and especially in technologies that show relevant competitive advantage.

An example of this trend was the participation of the investment fund KdT Ventures, based in the United States, in the recent investment round of the Chilean company Andes Ag. There are also exceptional cases of international players specialized in a vertical with an active presence in the region, such as AgFunder and The Yield Lab, which focus mainly on Biotechnology applied to Agriculture.

#### zentynel

#### **BIOTECH IN LATIN AMERICA**

- (10) https://vegconomist.com/startups/ michroma-creating-vegan-and-sustainablebio-colorants-to-disrupt-syntheticpetroleum-based-colourants/
- (11) https://indiebio.co/caspr-biotechrevolutionizing-molecular-diagnostics/
- (12) https://www.cienciavida.org/
- (13) https://biotechtown.com/en/home-en/
- (14) https://biotechtown.com/en/for-investors/

Finally, it is important to mention the role played by other agents such as accelerators and Innovation Centers: One of the most relevant is GridX, based in Buenos Aires founded in 2017 and Fundación Ciencia & Vida<sup>12</sup> in Chile, and Vida and Biotechtown<sup>13</sup> in Belo Horizonte, Brazil stand out.

Founded in 2018, Biotechtown seeks to unite science with business in the Life Sciences. It offers a 12-month incubation program and investments of between US \$ 50K to US \$ 150K, having to date 13 companies in its portfolio<sup>14</sup>.

#### **OUTSTANDING INVESTORS IN BIOTECHNOLOGY:**

#### Grid X

Company builder that starts from a premise; unite scientists with entrepreneurs who have specialized in business and can find a market for that idea. GridX is touring the country, visiting universities, laboratories and research institutes to map projects with the potential to become a company. Preselect 100 ideas per year, from which 20 are chosen to participate in an immersion program in the startup world. In parallel, it seeks young people from the business world, entrepreneurs, who are interested in venturing into the world of Biotechnology. Once teams are formed, their investment tickets are around US \$ 200K.

Operational partners: Matías Peire, page number 41.

#### CITES

It is a science-based accelerator formed by the Sancor Seguros Group based in Sunchales, Santa Fe province, Argentina. The investment focus ranges from Biotechnology, 3D technology, advanced materials and others. Among their value proposition, in addition to investment, there is infrastructure and laboratories in Santa Fe. They recently raised the first VC open fund in Argentina, CITES Financial Trust I, for a total of US \$ 24 million.

#### **SP Ventures**

Asset Manager based in Brazil, recently launched the AgVentures II fund with a focus on fostering new companies in the agricultural and food sector based in Latin America. Among its investors are BASF Venture Capital and Syngenta Ventures.

When reviewing the dynamics of investment in Biotechnology and the participation of investors in Latin America, three important elements can be highlighted:

- 1. There is no fund leading this industry, and the participation of the larger players (Kaszek, Monashees and others) is rather opportunistic.
- There is a large volume of investments in the early stages, and new players supporting the development of companies in the seed stage, which allows us to predict a good deal-flow for later stages.
- 3. Co-investment is becoming more common every day (almost 70% of the rounds were in co-investments), which is very relevant, since there would be interest in participating in investment rounds by the other funds in case that there was a fund that is positioned as a leader in Biotechnology.

Fuente: Asociación Mexicana de Capital Privado, Asociación Colombiana de Fondos de Capital Privado, Asociación Argentina de Capital Privado, Emprendedor y Semilla, Asociación Peruana de Capital Semilla y Emprendedor, Asociación Chilena de venture Capital, CORFO, The Private Equity & Venture Capital InBrazil program.

#### Mexico\_ •

VC Fund:	36
Opportunistic in Biotech:	
Pure play Biotech:	0

#### Colombia\_ •

VC Fund:	
Opportunistic in Biotech:	
Pure play Biotech:	0

#### Perú\_ •

VC Fund:	
Opportunistic in Biotech:	
Pure play Biotech:	

#### Brazil\_•

VC Fund:	
Opportunistic in Biotech:	
Pure play Biotech:	

#### Chile\_ •

VC Fund:	2
Opportunistic in Biotech:	Ę
Pure play Biotech:	1

#### Argentina\_ •

VC Fund:	2
Opportunistic in Biotech:	6
Pure play Biotech:	2

(6) Aurus Bio is the only fund focused exclusively in biotechnology, and it is completely invested.





# 3 | BIOTECHNOLOGY

## **3.1\_** WHAT IS IT AND HOW DID WE GET HERE

Biotechnology is a discipline that focuses on the manipulation of living organisms through the enhancement or inhibition of certain characteristics of these organisms in order to solve biological problems and/or carry out processes more efficiently. However, this is a very broad view, since centuries of agriculture and animal breeding would qualify as Biotechnology by this definition.

A more modern understanding of Biotechnology is born from the union between Biology, Computing and Statistics, where the knowledge of the living sciences has been refined and enhanced through the power of calculation provided by modern computing and statistical analysis tools to create multiple innovations, ranging from new drugs, pest resistant crops, functional food ingredients and new industrial processes.

The beginnings of modern Biotechnology are around a key milestone for humanity; characterization of the structure of DNA. Made in 1953 by James Watson and Francis Crick, the publication of the famous double helix structure of deoxyribonucleic acid (or DNA)15, was the beginning of a race to understand human genetics and all living organisms, which today it is known as Genetic Engineering.

But Biotechnology began to gain relevance in the field of science in the 1970s, when one of the most ambitious projects in modern history began, DNA sequencing16, where for the first time mathematical algorithms and development of specific software for the analysis of genetic information, were applied.

From this application on, Biotechnology has become intrinsic to many aspects of modern science. The first computational technological developments for DNA exploration and experimentation were followed by new engineering techniques to design and create molecules, microorganisms, and cells; explore and decipher the functioning of genes; and create transgenic animals and plants.

A by-product of this scientific revolution was the creation and development of new disciplines related to Computing and Biology, such as Bioinformatics, Biochemistry and Molecular Biology. But so was the proliferation of commercial and industrial applications that led to the creation and disruption of multiple industries.

- (15) https://www.nature.com/scitable/topicpage/ discovery-of-dna-structure-and-functionwatson-397/
- (16) https://www.nature.com/scitable/topicpage/ dna-sequencing-technologies-key-to-thehuman-828/

# GENENTECH

It was the year 1973 when the researcher Herbert Boyer together with other researchers developed the first genetically modified molecule in a laboratory. The team developed a revolutionary technique, called genetic recombination, that allowed the production of modified molecules in a standardized and scalable way, which was impossible with the traditional method of the date, which was based on the harvesting of molecules from animal organs. But it was not until 3 years later, when Herbert Boyer received the call from Robert Swanson, a venture investor at the firm Klein & Perkins, that the Genentech company was formed, with the aim of bringing the molecules developed through genetic recombination to the market.

Genentech, derived from the union of the words "Genetic Engineering Technology", started with an initial capital of a thousand dollars and managed to produce synthetic insulin in 1979, the first human hormone to be produced artificially. Until then, insulin was harvested from the pancreas of cows and pigs. Thanks to this launch, Genentech became the world's first public biotechnology company in 1980.

After human insulin, Genentech managed to launch several revolutionary drugs to the market, which were considered as Blockbusters due to their sales levels. These technological and commercial successes motivated the Swiss giant Roche to buy the company at a valuation of more than US \$ 46 Bn. Today, Genentech, a Roche subsidiary, has more than 13,500 employees, more than 40 drugs on the market and more than 20,000 patents received.

## **3.2\_** PRESENT AND FUTURE OF BIOTECHNOLOGY

Klaus Schwab, CEO of the World Economic Forum, has stated that we are entering the 4th industrial revolution made up of the fusion of technologies that will blur the lines between the physical, digital and biological spheres. This will generate great advances in Biotechnology which will transform economies and societies, while helping to solve the main challenges that we currently face as humanity.

The convergence of these technologies will open a series of very important business opportunities based on biological innovations in areas such as:

Medicine and human health: applications include cell, genetic and RNA therapies to treat or even prevent diseases, anti-aging treatments, innovations in reproductive medicine, improvements in drug development and assimilation, new predictive models of human health and diseases.

Agriculture, aquaculture and food: Applications in this domain include new ways of driving the reproduction of animals and plants, new more precise tools of genetic engineering of plants, effective use of the microbiome of plants, soil, animals and water to improve the quality and productivity of agricultural production, and the development of alternative proteins.

Consumer Products and Service: Applications in this domain include genetic testing, direct-to-consumer beauty and personal care solutions based on knowledge of the microbiome, and innovative approaches to the fitness of both humans and pets.

Materials and energy production: New biological ways of producing and processing materials, chemicals, and energy can transform many industries and our daily lives.

In a recent report by the consulting firm McKinsey17, it is estimated that the direct global annual impact of this so-called "Bio Revolution" could reach US \$ 2 to US \$ 4 trillion in 2030 to 2040, that is, between 6.5 and 13 times Chile's18 annual GDP, in the next decade. This impact is explained, among other factors, by the estimate that 60% of world production can be produced by biological processes and 45% of the world's disease burden could be addressed.

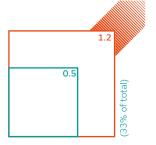
Advances in biological and computational sciences are currently being applied in multiple industries and being adopted in new fields of the world economy. Some notable examples of industries that have already embraced new biotechnology-based solutions are Agriculture and Medicine. In the first case, Biotechnology has allowed the development of crop varieties with greater resistance to droughts and diseases using bacteria and other microorganisms; improve the nutritional quality of crops and the early detection of diseases in livestock animals. In the same way, medicine discovery techniques, antibiotics and disease diagnosis have been revolutionized. (17) McKinsey Global Institue: The Bio Revolution: Innovations transforming economies, societies and our lives. May 13, 2020

(18) Banco Central de Chile



#### Biomolecules and Biosystems: \$1.7 - 3.4 (95% of total)

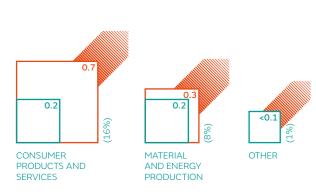
McKinsey report estimates the impact of the biotech revolution from US\$ 1.7 to 3.4 B, and more of half of it will be in health and agriculture.



HUMAN HEALTH AND PERFORMANCE



AQUACUULTURE, AND FOOD



Although the impact of Biotechnology is global, it has been especially important in certain specific regions, in which the cities of Boston and San Francisco in the United States stand out; the "Golden Triangle" of London, Oxford and Cambridge in the United Kingdom; and the "Biovalley" formed in the region linking France, Switzerland and Germany. The impact of Biotechnology in these regions has been more than just economic, since it has allowed the development of state-of-the-art medical centers, financed large university research projects and enhanced innovation ecosystems.



The Biotechnology industry in Massachusetts emerged in the 1980s, attracted by prestigious universities such as Harvard and MIT, favorable state regulations for biological research, and hospitals of excellence. Biotechnology ventures were appearing as a result of research, migrating from other regions and the same universities and laboratories were born from within.

These startups were concentrated in two main cities: Boston and Cambridge, separated by the Charles River.

This concentration of companies, which culminates in Kendall Square, a neighborhood known as "the most innovative square mile in the world" for having more than 25 companies and institutions including Amgen, Novartis Institute for Biomedical Research and Pfizer, has generated an innovation ecosystem where there are currently more than 430 Biotechnology companies.

The impact of this Industry on the Massachusetts economy is remarkable, generating more than 70,000 jobs in Biotechnology and Pharmaceutical companies, which translates into annual salaries of approximately US \$ 12 billion. On the other hand, during 2018, 18 IPOs of biotechnology companies in Massachusetts were carried out for more than US \$ 2.4 billion19.

But the impact in Massachusetts has not only been economic, but in several areas in which research, health and innovation stand out. On the research side, in the State there are more than 30 million square feet of laboratories and there are more than 120 universities and higher education centers. In Health, Biotechnology research has allowed Massachusetts to be the State that has obtained the most funds for its medical centers in the last 24 years and in the United States alone, more than 265 million patients have been treated with therapies developed in companies based on Massachusetts.

Finally, the economic development of Biotechnology has permeated different innovation industries, thanks to the regulation developed, the critical mass of investors and educational quality, which has allowed the creation of a multidisciplinary innovation pole, that granted Boston startups in 2018 to raise more than US \$ 8.8 billion in private venture capital.

THE IMPACT OF BIOTECHNOLOGY IN BOSTON

(19) Massachusetts Biotechnology Council 2019 Industry Snapshot.

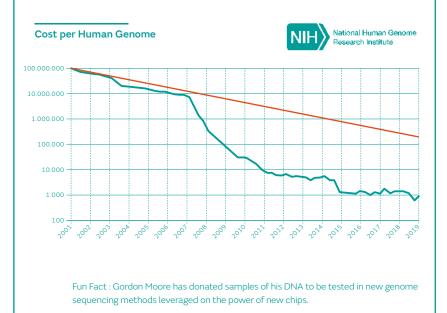
<sup>(20)</sup> Massachusetts Biotechnology Council 2019 Industry Snapshot.

# MOORE'S LAW

Advances in the field of Genomics over the past 25 years have led to substantial reductions in the cost of performing genome sequencing, a process by which the complete DNA sequence of an organism is determined. If in the beginning the cost was greater than US \$ 100 million, today it is less than US \$ 1,00021. This phenomenon is explained to a greater extent by advances in information processing, the availability of the necessary reactive chemicals and the greater supply of necessary equipment (hardware).

This trend in cost reduction reminds us of the famous "Moore's Law", a popular projection based on the statements made by the engineer Gordon Moore in 1965. Moore, after observing the advances in the processing capacity of the computers of at the time, it established that the processing capacity of computer chips per dollar would double approximately every two years, which would considerably reduce the cost of computing. This observation became one of the best predictions for the exponential growth of computational power that has been experienced since the late 20th century to date. The parallelism between reducing the cost of genome sequencing and computing power is also reflected in the simplification of both processes, from large laboratories and sophisticated computer equipment to home kits and smartphones.

On the other hand, in recent years the biological version of "Moore's Law" has surpassed the original. The National Human Genome Research Institute (NHGRI) claims that advances in genomics are outpacing advances in computing22. These advances have further accelerated the cost reduction of performing genome sequencing, where even in recent months the Chinese giant BGI announced that it is capable of doing this for less than \$ 10023.



- (21) https://www.genome.gov/about-genomics/ fact-sheets/DNA-Sequencing-Costs-Data
- (22) https://link.springer.com/content/ pdf/10.1007/s10739-018-9539-6.pdf
- (23) https://www.technologyreview. com/2020/02/26/905658/china-bgi-100dollar-genome/

#### **3.3\_** BIOTECHNOLOGY IN LATIN AMERICA

The Biotechnology revolution is a phenomenon that is happening all over the world and Latin America is no exception. Although the region is at an earlier stage when compared with the more developed regions mentioned above, there are several reasons that have allowed the agile development of this science in Latin America and competitive advantages that allow the region to project itself as a benchmark in this industry.

In the first place, the governments of the region have identified the value of this industry both in economic development and in solving social problems, which has been reflected in an active role in both legislation and investment. Examples of this are the Interministerial Agreement for the Development of the Argentine Bioeconomy signed in 2017. In Brazil, the Bioeconomy is defined as a strategic area in the National Strategy for Science, Technology and Innovation and the State of Sao Paulo has been a relevant actor with its project "Public Policies for the Development of the Bioeconomy". In Chile, the legislation on intellectual and industrial property stands out, which has emulated international standards and direct investment through state bodies such as "CORFO" and the "Fund for the Promotion of Scientific and Technological Development"

Second, Latin America and the Caribbean have 40% of the planet's biodiversity and historically it has had large reserves of natural resources. These resources allow the region to have a wide variety and quantity of resources necessary for scientific research and production of higher value goods based on Biotechnological techniques.

Another reason that is promoting the development of Biotechnology in Latin America is the quality of human capital that the different countries have in key disciplines of the life sciences such as Biology, Genomics, Biochemistry, Medicine, and Agricultural and Veterinary Sciences. The quality of human capital can be observed in the "Nature Impact Index 2019" which highlights the impact that the publications of scientific papers from Latin America in life sciences are having. Furthermore, this human capital is relatively cheap compared to the cost of human capital in more developed countries.

An example of this is the difference in average salary of professionals related to life sciences where, according to the "Life Science Salary Survey 2017", Latin America is 35% lower than that of Europe and 65% lower than that of the United States.

# CHIRON

In 1980 William Rutter, Pablo Valenzuela, and Edward Penhoet met in San Francisco to found the Chiron Corporation. The goal was to use genetic engineering to develop solutions to combat infectious diseases. By studying the genes of different viruses, they were able to identify proteins and markers to build tests and detection systems. One of its successes was to facilitate blood transfusion, by developing a test to identify the non-A non-B virus (HNANB or hepatitis C), which was known to exist but little information was available (and much less detection models). This advance allowed blood transfusion to be much safer and more widely used. They also developed the hepatitis B vaccine. This vaccine was one of the first to use recombinant DNA technology. This technique consists of isolating a DNA fragment and insert it into another genetic construct, which is capable of multiplying autonomously when inserted into a cell. DNA fragments will have the ability to produce antigenic proteins, that is, proteins of the microorganism to be vaccinated, generating the memory that allows an immune response.

Among the company's achievements is the industrial-scale development of insulin and the first sequencing of the HIV genome.

Chiron's strategy was to generate new developments in markets where there were no dominant leaders. With cutting-edge technology, innovative solutions and a light and simple structure, they achieved the attention of large corporations such as Thicon, Merck and Ciba Geigy, establishing partnerships and allowing their development to reach the market.

In 2006, and after more than 26 years of development and partnerships, Chiron was acquired by Novartis through a share purchase agreement that valued the company at approximately US \$ 9 billion.



### 4. THE BIOTECHNOLOGY INDUSTRY

### **4.1\_** INDUSTRY RELATIONSHIPS

Life sciences will transform economies, societies, and our lives. To support this transformation, it is necessary to invest resources in technological ventures that are at the confluence of advances in the life sciences and the development of processing capacity and artificial intelligence. These ventures will promote from the Biotechnology industry a new wave of innovation in a) Medicine and human well-being, b) agriculture and food, c) consumer products, d) and the industrial production of materials and energy.

It is important to note that the Biotechnology industry differs from other industries due to the high investment volumes and time involved prior to being able to bring a product or service to the market, due to the tests and certifications that are required. On the other hand, given the very nature of biotechnological innovations, products and services usually have a global applicability. These factors have profound implications for the investment in Biotechnology:

- Market risks are different from those of other technology ventures.
   While ventures related to innovative Information Technology solutions assume high risk over the potential market and their adoption by customers. The market risk in Biote is usually less uncertain, as the main challenge is their technology risk
- The risks associated with Biotechnology investments vary depending on the stage of each project. In early stages, the risks are related to the underlying technology and the appropriability (intellectual property strategy) of the solution, while, in more advanced stages, the nature of the risks is related to compliance with the testing and regulated processes.
- The protection of intellectual property is essential in order to capture the value invested in research and development.
- It is very important to have a broad knowledge of the Biotechnology business and a deep knowledge of the technological aspects associated with the biological sciences to understand the technological risks, applicability of the solution, novelty of the solution (and its appropriability), and know how to navigate through the approval process of the corresponding regulatory entities, a stage that is essential for this type of project.
- The network of contacts is key to attracting new investors, collaborators and specialized advisers, as well as to achieve attractive commercial associations or agreements for distribution.

Although risk factors are common to all potential solutions in the Biotechnology industry, it is in Bio-Pharmaceuticals, where these concepts become even more relevant due to its scale and complexity.

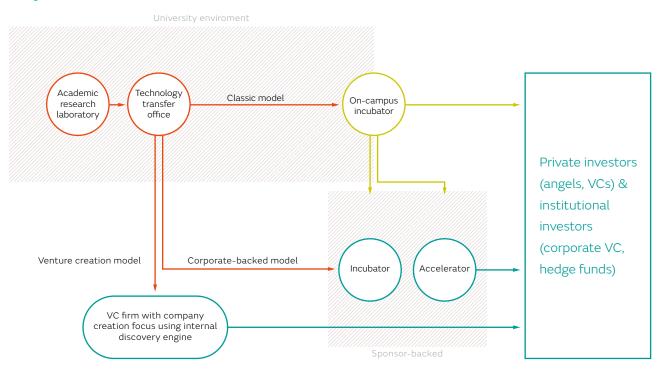
#### **4.2\_** VALUE CHAIN OF BIOTECHNOLOGY BUSINESSES

The great disruption in the Biomedical VC industry occurred in 1976 with the creation of Genentech, the first company that was able to synthesize insulin and produce it in a scalable way at a much lower cost than its competitors. Its founders raised US \$ 35 million from investors and funds, reaching a value of US \$ 300 million at the time of going public. That was the kickoff for a model that has grown dramatically since then.

Since then, three business creation models have predominated to achieve the commercialization of technologies; the classical model, based on the work of the technology transfer offices (TTO) of the universities; corporate incubators and accelerators, and VC funds with a specific focus or industry.

#### Research commercialization pathways

#### PitchBook Analyst Note: Betting on Biotech Q3 2020"



#### **BIOTECH IN LATIN AMERICA**

In the classical model, the TTOs of the universities are concerned with protecting the intellectual property of the innovations . This is key, as it must be done prior to the publication of any paper or document, and it is the foundation for the future of a company company. Without patents is very hard to raise funding.

A second model for the creation of Biotech companies is similar to model of the previous one, but generally includes the participation of a large corporation (Big Biotech and Pharmaceutical companies). The democratization of research and the lowering of costs to develop a biotech company allows research breakthroughs to emerge from places that do not necessarily have a critical mass. As such, entrepreneurs often face big problems attracting enough capital to expand their businesses. This is where the support of a large company can be a lifesaver, offering investment, networks of specialists and mentors, working capital and contacts for scaling up.

Finally, a third model has started to appear. Some Venture Capital funds have begun to focus on a particular industry problem or challenge (for example diagnostic tests or cures for orphan diseases). They carry out an in-depth review of the intellectual property existing in a specific market. Then , a team of founders with a track record in the industry and knowledge of the market is assembled.

An example of this model was the case of Magenta Therapeutics, which was co-founded and incubated by Atlas Ventures in 2015 to revolutionize stem cell transplantation as the new treatment paradigm for autoimmune and blood-borne diseases. In this case, where Atlas sought the technology from a problem raised thanks to its internal team and international networks and, it managed to carry out an IPO in just 3 years.

# GENEPRODX

Geneprodx is a classic example of a company supported by a Technology Transfer and Licensing Office.

The Biomedical Research Consortium-Chile (BRMC) was born in 2007 as a result of the association between the Pontificia Universidad Católica de Chile, the Recalcine Pharmaceutical Corporation and other important companies in the Pharmaceutical area, with the aim of developing high impact products for human health . Thyroid Print, a test based on 10 biomarkers for the detection of thyroid cancer, was developed from the work of the group led by Dr. Hernán Gonzalez. These data combined with an algorithm allows to determine whether a nodule is carcinogenic or not. The University filed a patent application in 2013. Subsequently, the University out-licensed the patent to Geneprodx Spa, a company founded in 2015 by Dr. Gonzalez and his team. With a first raise of US \$ 2 million, the company began the tests in Chile to validate the technology . To date, Geneprodx has raised more than US \$ 6 million , carried out more than 500 tests globally, published a series of papers , and already has a commercial operation in Chile.

# PHAGE

Phage is a biotech company focused on creating new feeds and foods for animal and human consumption. Its first product, launched in 2014, was a feed additive that aimed to prevent neonatal diarrhea in calves, a disease that reduces the weight and size of animals. For this, they were supported by of the Ciencia & Vida Foundation, which provided funds, facilities and know-how . They also had financing from the Startup Chile business incubator. With all this, they managed to increase production and reach the first sales, which caught the attention of Bayer Animal Health , signing an agreement for the distribution and sale of the product in 2016. With this, Phage managed to scale globally, closing a round for US \$ 4 million in 2019 and start operations in Europe.



# 5. ZENTYNEL VC

Biotechnology ventures in Latin America face a significant challenge when they seek to raise rounds of between US \$ 2 MM and US \$ 7 MM. This is due to the absence of specialized investors capable of evaluating, among other things, the risks and potential of the technology, the intellectual protection strategy, the market potential and the challenges to achieve an exit.

Zentynel emerges as a "convergent evolution" between the Ciencia & Vida Foundation and Venturance Alternative Assets, which, coming from different industries, identified the need for Biotechnology companies to have a specialized investor, as well as an opportunity to contribute both capital and experience, in order to accelerate the development and growth of this type of initiative in the region.

# 5.1\_ GENESIS OF ZENTYNEL

Venturance Alternative Assets is an investment fund manager specialized in alternative assets, which in 2017 created the FIP Alerce VC fund. Since then, the Alerce fund has invested in 16 early-stage ventures, of which 10 are related to the Biotechnology area.

The foray into the area of Biotechnology led the Alerce Fund team to cross paths with one of the main references in this industry, the Ciencia & Vida Foundation. This center, founded in 1996, brings together more than 200 scientists, has been the cradle of more than 30 ventures and has raised funds for more than US \$ 60 million. The interaction with the Foundation team that include Pablo Valenzuela, Bernardita Méndez and Cristián Hernández in various boards and committees, ended up consolidating a common motivation around building a Biotechnology industry in Chile.



Pablo Fernández MSc

Roberto Loehnert MBA

MBE

Cristián Hernández PhD

Bernardita Méndez Pablo Valenzuela PhD

Zentynel was born from this common vision to jointly develop a VC fund specialized in Biotechnology in Latin America. The complementarity skills and shared vision, not only of the potential of the business, but especially of the values and culture of the teams, allowed the development of a work plan in just months. This is how in January 2020 it was agreed to form a joint venture, Zentynel Frontier Investments, to develop the first Latin American fund focused exclusively on Biotechnology: Zentynel I.

Zentynel Frontier Investments seeks to be the convergence of two worlds; investment and innovation in Biotechnology, and the name reflects the character of "seeking" opportunities on the frontier, expanding knowledge.

#### zentynel

**BIOTECH IN LATIN AMERICA** 

## Venturance Alternative Assets

Venturance is a company specialized in real investments focused on the creation of value through the active and dynamic management of its portfolio. Its three partners have participated in the management and direction of more than 30 companies for more than 12 years.

The company has two main areas, the Administration of Investment Funds and Financial Advisors. Both areas share market knowledge, good practices and allow clients to be given complete attention to their assets.

Within the Administration of Investment Funds there are 4 areas defined by the investment focuses of each one. These areas are Private Equity, with a focus on investment in medium-sized companies through active management and resources that allow scaling and optimization of businesses, Venture Capital, which seeks to invest in technological solutions for large industries and with great potential for escalation, Private Debt, which invests in debt instruments linked to small and medium Chilean companies and Real Estate, which participates in real estate development projects in Chile and abroad, through partnerships with the main real estate developers in the region.

On the other hand, the Venturance Financial Advisory area supports its clients in the development of business models, implementing management control programs and operational excellence, advising on tax planning and reorganization of companies and in the administration of high assets.

More than 10 years of experience in the Chilean market and a team made up of more than 25 highly qualified professionals with different profiles, have allowed Venturance to become one of the leaders in Alternative Assets, with more than US \$ 250 million of equity administered.

## **CIENCIA & VIDA FOUNDATION**

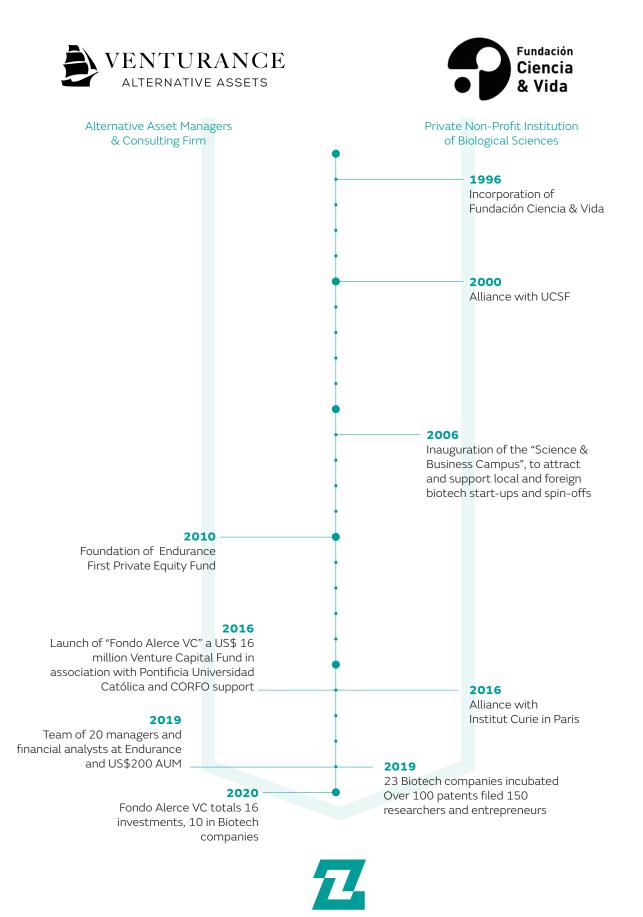
Ciencia & Vida Foundation is a private, non-profit institution whose objective is to improve the social and economic development of Chile through scientific discovery, entrepreneurship and education in biological sciences.

After having co-founded one of the world's largest biotechnology firms in the United States, Chiron Corporation, Pablo Valenzuela headed to his native Chile and founded the Ciencia & Vida Foundation in 1996 with Bernardita Méndez and Mario Rosemblatt.

The idea from the beginning was to create a bridge institution that would connect academia and industry and foster interaction between scientists, entrepreneurs, students, and communicators. Over the years, Ciencia & Vida Foundation has evolved into an integrated platform for research, discovery, advanced training, global science, entrepreneurship, and outreach.

As a small independent center, the Ciencia & Vida Foundation structure does not have many levels of hierarchical authorities. The organization is fairly horizontal and includes people with experience in entrepreneurship, business, intellectual property, and technology transfer.

Currently, the Foundation has 12 specific research groups in life sciences and applied technology and more than 200 professionals related to science work.



# **5.2\_** ZENTYNEL TEAM

#### **GENERAL PARTNERS**

Zentynel is led by a team of General Partners (GPs) that include Pablo Valenzuela, Bernardita Méndez, Cristián Hernández, Pablo Fernández and Roberto Loehnert.



### Pablo Fernández, Msc

With more than 10 years of experience working in the development of innovations and ventures, Pablo is currently Manager

of the Venture Capital area of Venturance and portfolio manager of the Alerce VC fund. Pablo participates in various directories such as Andes Ag, GeneproDx, Done Properly, Polynatural, Z-Data Lab.



#### Cristián Hernández, MBE

He has over 17 years of experience in the investment and development of Biotechnology companies and additionally, he has been General

Manager of 3 biotechnological enterprises. Cristián is a member of the Board of Directors of Ciencia & Vida Foundation, Nova Mineralis, Science Heaven, Ingalfarma, Phage Technologies, The Network Factory and GeneproDx.



#### Roberto Loehnert, мва

He has more than 12 years of experience in investment and development of startups and growing companies. He was General Manager

of EFT Group and is a founding partner of Venturance Alternative Assets where he currently leads the VC area. Roberto is a member of various Boards including Clínica Alemana de Santiago, Bbosch, Lippi and Streat Burger.



#### Pablo Valenzuela, PHD

Dr. Valenzuela has more than 35 years of experience in the investment and development of Biotechnology companies. He was

the developer of the hepatitis B vaccine, discoverer of hepatitis C and has more than 50 patents to his credit. He was a co-founder of Chiron, which was later sold to Novartis for \$ 8.9 billion. Currently Dr. Valenzuela is President of Andes Biotechnologies and is a member of various boards of directors including Nova Mineralis, Andes Ag and the Universidad San Sebastián.



### Bernardita Méndez, рно

Dr. Méndez has solid biotechnology experience having spent more than 10 years at Chiron in various positions including Vice President of Regulatory Issues and Quality and

has led more than 10 approval processes before the FDA. She is currently President and co-founder of the Ciencia & Vida Foundation and participates in boards such as Fundación Chile, Universidad Andres Bello and Comunidad Mujer.

#### ADVISORS

Zentynel has a powerful group of advisors made up of Les Funtleyder, Juan Andrés Camus, Henrique Martins and César Hidalgo, who provide valuable help and guidance, complementing the team of GPs with distinctive skills that are key to the success of the project.



## Les Funtleyder

Investment Manager at E Squared Capital, Investment Fund in New York. Responsible for leading fundamental analysis and valuations of public and private companies in the Health industry. Author of the book "Healthcare Investing".



### Henrique Martins

Henrique is Portuguese, Medical (internist), with a Master's and Doctorate in Management (U of Cambridge) and other postgraduate degrees in HIV and Law. He was president of the eHealth Services of the Portuguese Ministry of Health for more than 7 years and led all the joint action efforts of the more than 27 Member States of the European Community to implement the eHealth standards in Europe.



#### Juan Andrés Camus

President of the Santiago Stock Exchange, founder of Celfin Capital and leader of growth until consolidating it as an icon of investment banking in Chile. Director of several leading organizations and NGOs in Chile such as CCLV and Centro de Estudios Públicos (CEP).



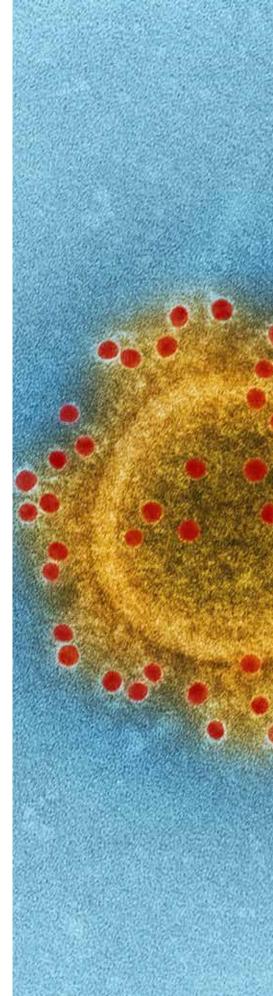
### César Hidalgo

ANITI Chair at the University of Toulouse, Honorary Professor at the University of Manchester, and Visiting Professor at the Harvard Faculty of Engineering and Applied Sciences. Founder of Datawheel, Data visualization and distribution company. He was a professor at MIT Media Lab, He received the Lagrange award in 2018.



### Guillermo Emrich

Partner at FIR Capital. He has extensive experience in business management in the roles of CEO and / or Chairman, or as a member of the Board and Advisory Boards. He worked in these roles at Biobrás S / A and Biomm S / A, Holcim, Cedro Cachoeira, Fundação Biominas and at CSEM Brasil. For four consecutive presidential terms, he was a member of the National Council of Science and Technology, chaired by the Presidents of the Republic.



#### **OPERATIONAL PARTNERS**

With the purpose of being a truly Latin American biotech fund, Zentynel has strengthened the team by recruiting Operational Partners in the main hubs in the region. Operational Partners are leading professionals in the world of VC in Biotechnology in their respective regions, and they have a key role in publicizing the fund in the ecosystem, identifying potential ventures, materializing investments and supporting the management of the investment portfolio of the region.

The Operational Partners by country are the following:

# Eduardo Emrich

#### BRAZIL

Since August 2003 he has been the President and CEO of Biominas. He has more than 25 years of experience identifying and analyzing opportunities in the world of Biotechnology, in addition to promoting and supporting projects in the Life Science industry. He has a degree in Biological Sciences with a major in Biochemistry and Molecular Biology from the University of Minas Gerais and a postgraduate degree in Administration from the Getulio Vargas Foundation.

#### Matías Peire ARGENTINA

Founder and CEO of GridX, the first company builder focused on Biotechnology in Latin America. After 15 years in the world of technological entrepreneurship, and after a stint at Singularity University, Matías founds Gridx in order to turn biotechnological developments into companies with global reach. Matías has a degree in business from the University of Buenos Aires.

#### Ramphis Castro **CENTRO AMÉRICA**

He is an entrepreneur, investor and director of ScienceVest, a first-check fund focused on the areas of robotics, artificial intelligence, synthetic biology, genomics, space, among other areas of advanced technologies. Ramphis has degrees in computer engineering, law and finance and is part of the YCombinator and Kauffman Fellows network. He is originally from Guayama, Puerto Rico.

#### Cármen Contreras COLOMBIA

Carmen has a Phd from Oxford University and is associated with the Technology and Management Centre for Development from the same university. She has been a consultant for the Interamerican Development Bank and the World Bank. Since 2007 her has focused to study and understand the different dynamics of the innovation and entrepreneurship ecosystem in Latam, with a special interest in the creation of Biotech startups.

# **5.3\_** TRACK RECORD EXPERIENCE

Zentynel brings together a powerful team with complementary capabilities that has a deep understanding of the technical, regulatory and interpersonal complexities of the Latin American Biotechnology industry. The team members have participated and led various investments in Biotechnology such as:





These companies have met outstanding milestones, including protecting their Intellectual property, obtaining FDA approval, developing R&D facilities as well as manufacturing facilities, conducting clinical trials in Chile and the US, and signing association and distribution agreements with global players in the Industry.

Advances in life sciences will transform economies and societies, while helping to solve the main challenges we currently face from climate impacts to pandemics such as this crisis. We believe that this fund can have a very relevant impact for Chile and Latin America. Zentynel Frontier Investments seeks to provide financial and managerial support to entrepreneurs who are redefining food production, developing medicines for the future, and supporting novel industrial processes.

