LifeLink Ventures

2021 Annual Biotech Report

We wish to connect private investors with emerging technologies that address global health challenges. To do so, first we must bring our investors closer to the biotech world

Foreword

"We see LifeLink as our commitment to medicine and science, and we are in it for the long run."

Francisca Peixoto, Investment Manager

LifeLink Ventures is an investment company led by private investors. Through LifeLink, they find a doorway to **investments with the power to improve lives**.

We focus on early-stage biotech / biopharma startups targeting urgently needed therapies. The development of a new treatment takes many years - the time from patent filing to commercial launch averages 13 years (IQVIA, 2017); therefore, we focus on problems that will unfortunately affect humanity for the upcoming 30-50 years. These health issues are reflected as **macrotrends that affect society as a whole** and include: the ageing population and association with neurodegeneration, increased incidence of obesity and association with metabolic dysfunction and inflammation and the growing need for treatments against infectious diseases.

While healthcare in general still faces major challenges, **we remain firm believers in the talent and drive of the leading scientists of our time and look forward to supporting them and their ideas in the years to come.**

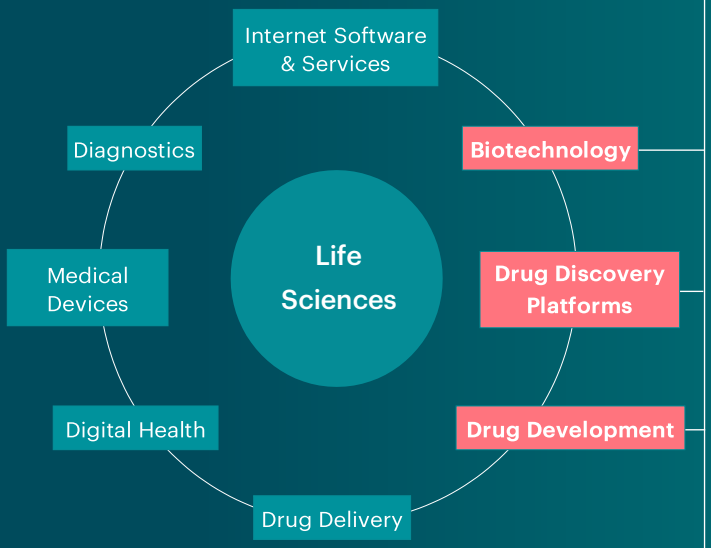
As always, we welcome feedback and encourage discussions with our investors about the implications of our observations.

Leo Figueiredo
Co-founder &
Executive Chairman

Francisca Peixoto, PhD, MBA
Co-founder &
Investment Manager

LifeLink Ventures

Life Science encompasses multiple technological fields. **Our main areas of focus are:**



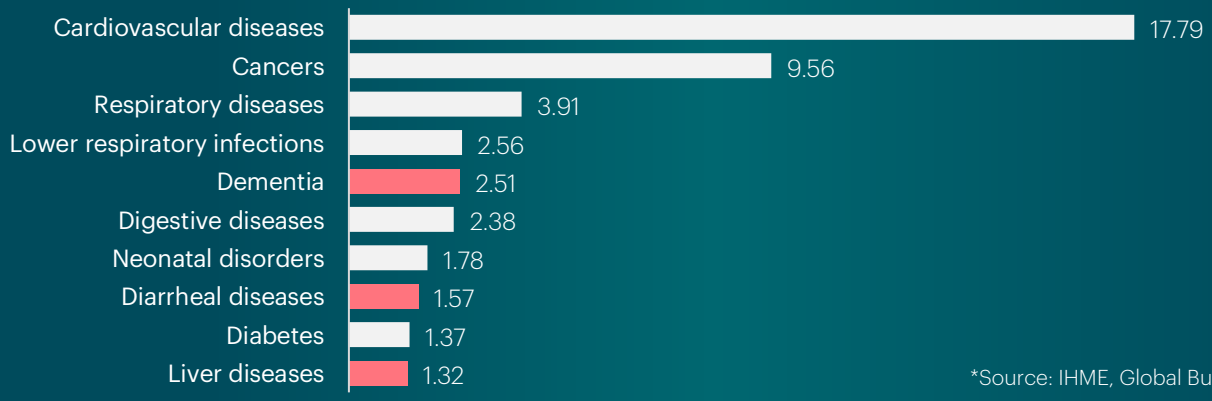
These include different types of therapies:

- **Small molecules** (chemically synthesized)
  Examples: paracetamol, ibuprofen, chemotherapies

- **Biologics / Advanced therapies** (extracted or engineered from living organisms)
  Examples:
  - Vaccines
  - Gene therapies
  - RNA therapies
  - Antibodies
  - Cell therapies
  - Oncolytic virus therapies
  - Etc.

Our portfolio companies focus on key global health issues. Examples in our portfolio include Eveliqure, developing a novel vaccine against bacteria responsible for diarrheal diseases; Ochre Bio, developing treatments for liver disease; and Aleva Neurotherapeutics, developing a medical device for Parkinson's. We continue to explore other fields such as oncology and cardiovascular disease in search for novel therapeutics.

Number of deaths (in Millions) by cause, World, 2017



*Source: IHME, Global Burden of Disease

2021 Annual Biotech Report

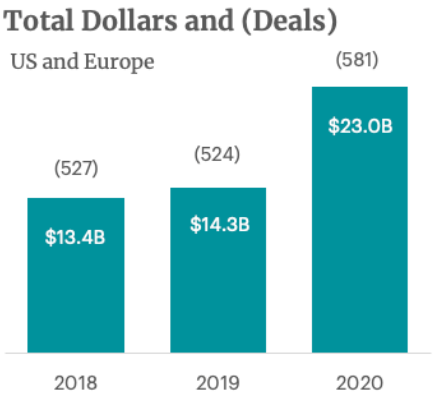
Highlights

LifeLink

1. The biotech sector keeps growing

Deals

Biotech and biopharma continue to grow. In 2020, the number of deals and capital invested hit new records. US biotech led on investments, while Europe's mean funding size grew at more than twice the rate of the US. In China, the number of funding rounds grew four times faster than in Europe or the US.



*Source: BCIQ

IPO activity has grown faster than any other category of fundraising, with companies raising over $25 billion this year and $20.5 billion in 2020, a massive increase over the $7.9 billion raised in 2019 (source: PitchBook).

Public biotech and biopharma companies in numbers (source: PitchBook):

10% of all public companies on Nasdaq
(excl. medical devices and digital health/services)

→ *+5T USD* in value

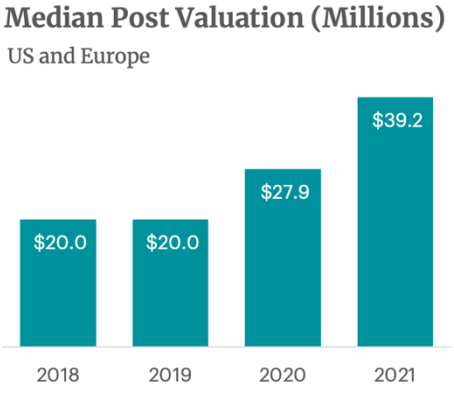
1.6B USD average market cap
(excl. outliers like Moderna and large pharma)

→ *24%* of all public biotech/ biopharma cross the 1B mark

Valuations

Valuations in the sector have been increasing rapidly over the years, which requires investors to be selective with their capital. The graph below depicts the median post-valuation of life sciences companies that raised seed, series A or series B rounds (combined).

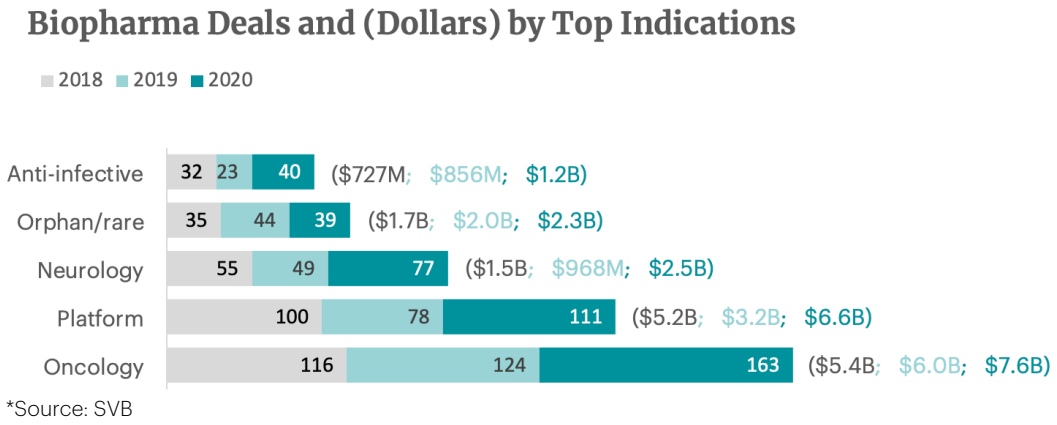
To maximize the future value of invested capital, **LifeLink** focuses on identifying promising technologies prior to the major pre-clinical inflection points. We also take a conservative approach in terms of ROI calculations to ensure there is space for relevant returns.



*Source: PitchBook

Areas of Investment

Oncology receives the majority of venture capital, however, the amount of capital invested in other areas and platform companies (those developing multiple assets for different diseases) has continued to grow significantly as well.



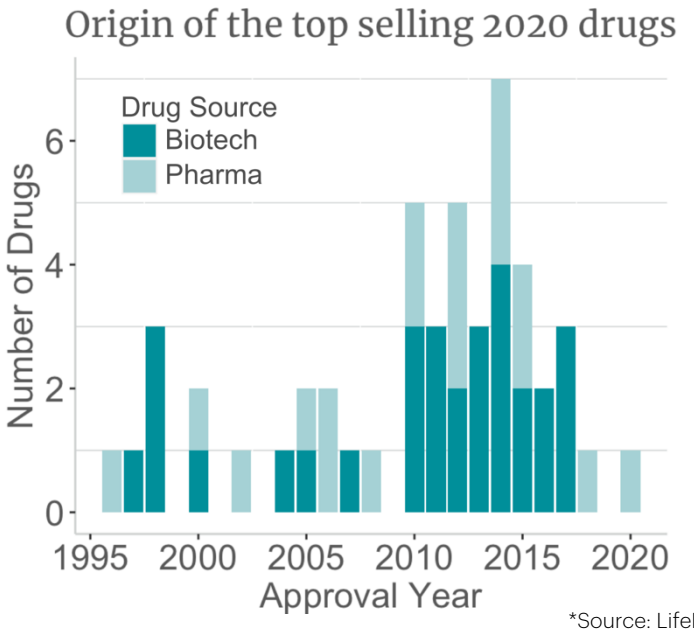
*Source: SVB

As a de-risking strategy, **LifeLink** sees value in platform companies and continues to bet on companies with technology capable of developing a pipeline of therapies, including Chameleon Biosciences and Ochre Bio.

2. Small biotechs – a key source of innovation

Smaller biotech companies continue to be a substantial source of innovation as it is common practice for large pharmaceutical companies to acquire products from biotechs after certain key development milestones.

60% of the 50 highest selling drugs of 2020 were originally developed by smaller biotechs. This high proportion highlights how dependent drug development is on the private capital directly supporting emerging companies.



*Source: LifeLink analysis

3. Why rare diseases are attracting VC money

Most rare diseases have no effective treatments. To incentivise their development, the US created the Orphan Drug Designation (later adopted in other markets including the EU). Orphan Drug Designation provides several economic advantages to companies developing drugs for rare diseases:

1. IP Protection: Approved drugs are protected from market competition for 7 years in the U.S. and 10 years in the E.U.
2. Fast-Track Approval: The FDA fast-tracks applicants for approval, waives certain fees, and helps with aspects of the application, such as writing protocols. In 2019, 44% of new FDA approvals went to orphan drugs, and the likelihood for success is higher than traditional drugs.
3. Less Pricing Restrictions: Companies with orphan drugs often charge higher prices with less challenge from insurance carriers.
4. Higher Revenues per Patient: After nearly 4 decades of relatively consistent growth, orphan drugs account for over 15% of worldwide prescription sales.
5. Lowering Testing Costs: Less time spent in pre-clinical and clinical testing translates, potentially, to millions of dollars saved in expenses. Finally, companies developing orphan drugs can receive tax benefits.

There are approximately 7,000 rare diseases (defined as fewer than 200,000 patients) affecting 400M patients worldwide (e.g.: cystic fibrosis, muscular dystrophy, Huntington's disease). Currently, there are only drugs available for approximately 5% of all rare diseases.

Venture investment in the rare disease space has skyrocketed, and pharma companies continue to grow their rare disease franchises. However, it is not uncommon for rare disease therapeutics to commercially be a "winner takes all" scenario. Furthermore, validating the commercial case for rare disease drugs can be challenging due to limited or unclear exclusivity periods and large undiagnosed populations.

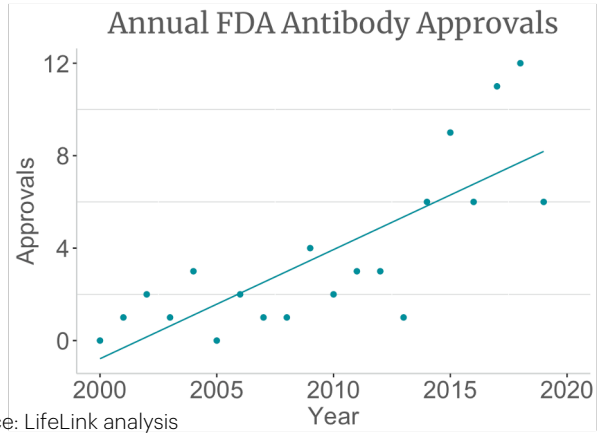
Chameleon Biosciences, one of our portfolio companies, is developing next generation gene therapies and applying it to the treatment of rare diseases.

4. Categories of therapeutics

The number of therapeutic modalities continues to diversify beyond traditional small molecules, highlighted by the increased approval of antibodies, pharma´s renewed interest in RNA and an increasing number of gene therapy clinical trials:

Antibodies

In the last two decades, antibody-based drugs have proven to be highly effective, specifically for cancer. **LifeLink** maintains interest in antibodies and is in active discussion with multiple companies developing them.



*Source: LifeLink analysis

RNA

Prior to the covid19 pandemic, RNA therapeutics primarily treated rare diseases. Given the success of Moderna and BioNTech, pharma is now interested in the wider therapeutic potential of RNA. Examples of two recent acquisitions:

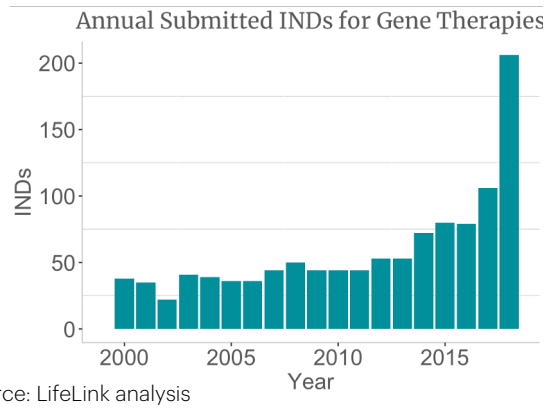
Novo Nordisk buys Dicerna → *$3.3 billion M&A*
Acquisition to buy pipeline of RNA therapeutics

Sanofi buys Translate Bio → *$3.2 billion M&A*
Acquisition to buy novel RNA vaccine platform

LifeLink expects RNA therapeutics to benefit large patient populations. This year, we joined the series A round of Ochre Bio**,** to support the development of a novel RNA therapeutics platform for liver dysfunction.

Gene Therapies

Clearer regulatory guidelines and improved manufacturing have increased the number of gene therapy trials. While the technology is validated, it still faces challenges regarding patient compatibility. This year, **LifeLink** participated in the seed round of Chameleon BioSciences, to support the development of universally patient compatible gene therapies.



*Source: LifeLink analysis

While the above modalities have seen substantial progress, small molecules continue to innovate, including new classes of highly tumor selective molecules[1]. Ultimately, diversification of biotech tools will continue to increase the number of diseases directly addressed with therapeutic interventions.

5. 2021 stories

Biogen's Controversy

In June 2021 the FDA approved a first of its kind treatment for **Alzheimer's disease**. The antibody, Aduhelm, received accelerated approval based on the clinical observation that it removes brain amyloid plaques. The accumulation of amyloid plaques in the brain has been correlated with Alzheimer's progression however, it remains unclear whether this is a cause or consequence of the disease and whether plaque removal results in improved cognitive outcomes. Therefore, the approval of Aduhelm has faced criticism from FDA advisors, clinicians, and biopharma insiders. Such criticism also arose from pricing considerations and safety concerns.

As part of the accelerated approval process, Biogen has a 9 year follow up period to confirm that Aduhelm improves patient cognitive outcomes. Because of the uncertainty surrounding the benefits of amyloid plaque removal, this approval sets a potentially dangerous precedent since it motivates others to pursue the same mechanism. Indeed, as of 2021, both Eli Lilly and Roche are clinically testing competitor antibodies with similar mechanisms of action, removal of amyloid plaques.

Precision Medicine for breast cancer

AstraZeneca/Daiichi-Sankyo developed a targeted therapeutic (Enhertu) for **metastatic breast cancer** that can be used by itself or in combination with chemotherapy. Enhertu is an antibody that physically delivers cytotoxic drugs to cancer cells, resulting in targeted tumor destruction with reduced toxicity to healthy tissues.
Designated a breakthrough therapy by the FDA, Enhertu was commercialized in 2020 and has drastically improved patient outcomes. In 2021 AstraZeneca reported a doubling of patients entering complete remission after treatment.

Theranos' Bad blood

Former Theranos' CEO Elizabeth Holmes is battling fraud charges after having raised nearly $1 billion in private equity. While the trial is ongoing, prosecutors suggested Holmes fabricated third party validation and misled investors about contracts with the US government. This unfortunate scenario highlights the importance of thorough diligence from specialized venture capital companies.

6. covid19 Therapeutics

Vaccines

Vaccines remain the most effective tools to curb the covid19 pandemic. Listed below is the efficacy of the given vaccine at preventing hospitalization (severe disease) and symptomatic covid19 (moderate / mild disease).

Company	Vaccine Type	Doses	Hospitalization	Symptomatic
Moderna	mRNA	2	>90%	>90%
Pfizer	mRNA	2	>90%	>90%
Johnson/Johnson	adenovirus	1	85%	65%
Astrazeneca	adenovirus	2	90%	63%
Sinovac	Inactivated SARS-CoV2	2	>90%	50%

Note: numbers summarize data from late-stage clinical trials and government regulators (FDA, EMA, WHO, NHS). These data are not specific to any individual variant and in some cases are averages of multiple reports, as efficacy values can vary depending on the length, size and time of a given study.

This data shows that many vaccines can reduce the social and economic burden of hospitals being overly crowded with covid19 patients but vary in the ability to prevent moderate / mild disease. The durability of these efficacy values will continue to be monitored over longer time periods.

Mix and Match

Due to the broad effectiveness of mRNA vaccines, regulators are determining if individuals who received non-RNA vaccines benefit from mRNA doses. Trials are ongoing (including a study in the Philippines combining Sinovac with 1 of 6 vaccines[2]) but initial data suggests the strategy is safe and efficacious[3].

Booster shots

Given the safety profile of covid19 vaccines and the emergence of variants of concern, many public health officials are recommending booster shots to provide additional security to individuals and further mitigate viral spread. At this moment the long-term immunological memory of vaccination is still being assessed and cannot solely be measured by antibody titers.

Oral anti-virals

Merck and Pfizer revealed positive clinical data for oral covid19 anti-virals. Molnupiravir (Merck) and Paxlovid (Pfizer) reportedly reduce hospitalization of high-risk patients by 30% and 89%, respectively. These antivirals are expected to notably reduce hospitalization due to their relative low cost and oral dosing.

7. Contact

For more information on LifeLink Ventures or our portfolio companies please reach out or visit our webpage:

Webpage: www.lifelinkventures.com

Email: info@lifelinkventures.com

Company: LifeLink Ventures Limited

Location: Barcelona, Spain

References

1 - Mirati triumphs again in KRAS-mutated lung cancer

2 - FDA reviews 4 brands for booster and additional shots, possible mix and match

3 - Mix-and-match COVID vaccines trigger potent immune response

LifeLink Ventures