



LUXOR
—
INVESTIMENTOS

Investors
Letter

April 2024



Manager's Message

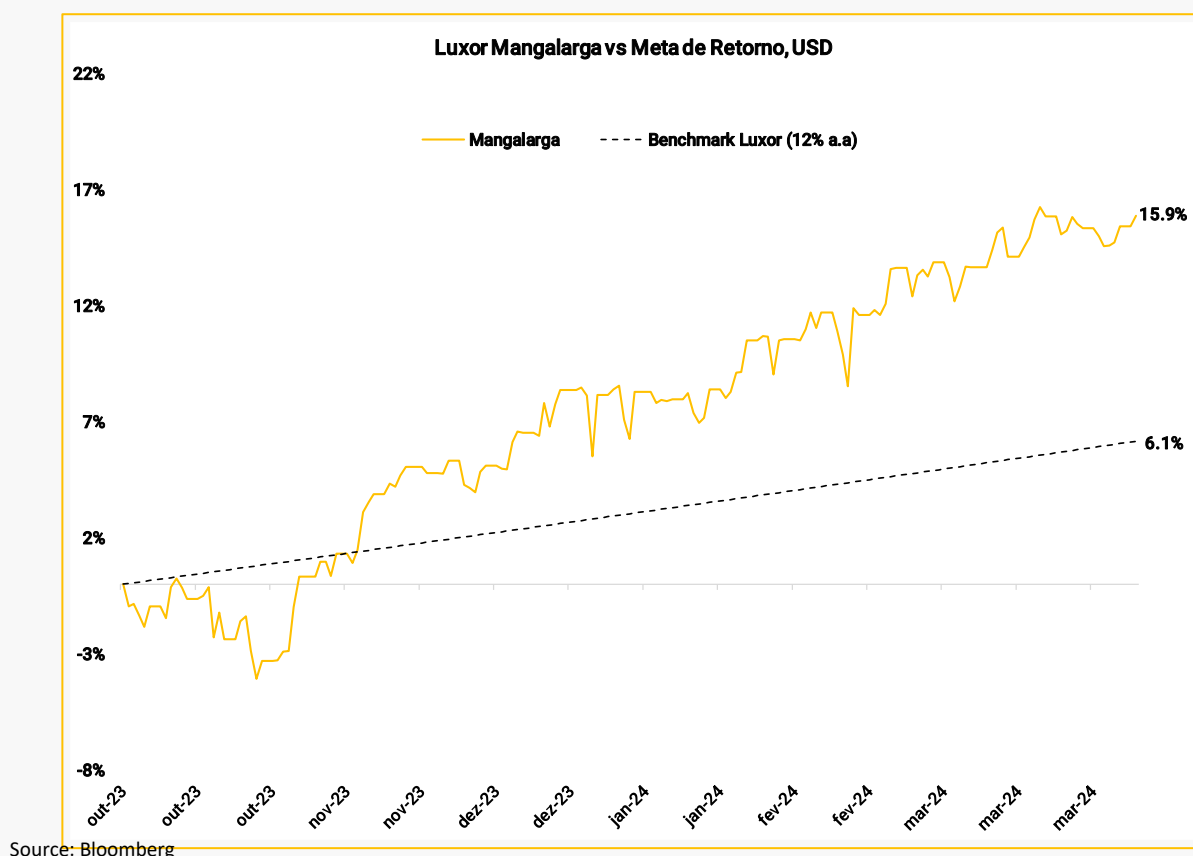
“One of the fundamental principles of our investment strategy is to identify exceptional companies that not only have solid competitive advantages but are also aligned with long-term trends. A notable example of the harmony between these elements in our portfolio are Danaher and Thermo Fisher. Both are companies of excellence, with robust competitive positions, and are being driven by the ongoing evolution in the treatment of chronic diseases, a trend we are closely monitoring. These companies are uniquely positioned to capitalize on the value created by treatment discoveries that enable humanity to further increase its longevity and quality of life.”



1. Update on Performance

As many know, Luxor works in 36-month cycles where we set goals and projects with the aim of moving towards the group's long-term objectives. In 2023, we concluded our most recent cycle and, throughout the year, we took the time to think about what we would like to achieve in this new triennium of 2024-2026 that begins. In this exercise, we also made some small internal adjustments. In particular, we would like to inform you that we have changed our target annual return on Mangalarga from US CPI + 6.5% to 12% in US dollars. In practical terms, this does not change our way of investing at all. Even so, we consider it important to inform that this will be the benchmark with which we will compare the fund's performance.

The last six months have seen significant gains for Mangalarga. Since September 2023, the fund has achieved a 16% return, primarily as a result of the performance of our stock portfolio, which gained 19% versus 22% for the S&P 500. It was a period in which the market as a whole had a recovery, largely due to the fall in the risk of global inflation and the end of the cycle of interest rate hikes in the US, in addition to good results of companies. Fortunately, most of the stocks in our portfolio fared even better than the S&P 500, which makes us particularly encouraged – even if the one-semester period is not long enough for us to make assessments of the performance of our investments.



2. Portfolio Update

Regarding the portfolio, little has changed in the last six months, except for the rebalancing that we are doing as opportunities arise and we deem appropriate. The biggest change that has taken place since the last letter was the divestment of Suzano. We have deep admiration for the company's managers and consider that the company is on a virtuous path, with an efficient operation capable of being profitable, even in a competitive industry, given its average cost of pulp production, well below the current estimated marginal cost in the world. However, our discomfort was due to the prospect of the entry of new producers in different geographies. We do not consider that we have the capacity to predict these movements, much less the exact impact of the entry of this additional production capacity on world pulp prices, in a context in which global demand for the input has grown predictably, but gradually.

On the other hand, we are glad to have recently invested in the Salta Group. It is one of the most successful business stories in Brazil in recent years, built in the important education sector. The business is led by three of the newest and most competent entrepreneurs in the country – Leila Orenstein, Rafaela Dantas and Duda Falcão, people we know, trust and admire. We are happy to join them in this endeavor and confident that the group will follow a path as virtuous as the one taken so far.

In our stock portfolio, we are investing again in Localiza, a company that we have been investing in for a long time in the past. Basically, since the acquisition of Unidas, we have

observed a significant improvement in Localiza's competitive position. However, with the worsening of the used car market and the rise in interest rates in Brazil, the company's result had a relevant drop that we consider to have a large temporary component, but which negatively impacted the company's share price. We consider that we are facing an interesting opportunity to acquire a stake in the company at an attractive price and with a long-term perspective even better than the one that existed at the time of our initial investment, understanding the risks inherent to Brazilian businesses.



2.1 Introduction

One of the elements of our philosophy is to look for companies whose growth is being driven by a secular trend. This does not mean that we look for companies based on these trends, but rather that this is an element that we consider throughout our process of searching for great deals and ultimately for returns. In this letter we will talk about the progress that humanity has achieved in the field of new treatments and vaccines, as well as the importance of secular trends in our allocation of capital.

2.2 What is a secular trend?

A secular trend refers to a process that unfolds over a considerable period of time and that causes profound transformations in the environment in which it occurs. These trends can be observed in various fields, including economics, epidemiology, demography, and technology. For example, in economics, a secular trend can refer to a prolonged period of economic growth or decline. In demography, it can refer to changes in birth rates or life expectancy over several decades. In epidemiology, a secular trend can be observed in the incidence or prevalence of a given disease over time. In technology, it can refer to the constant improvement or adoption of a particular technology over many years. Specific examples more directly linked to our investments are the gradual migration of commerce to the virtual environment (e-commerce), the digitization of means of

payment and the expansion of the memory and processing capacity of boards and chips in recent decades. Secular trends are important for understanding long-term patterns and making predictions about future developments in a specific area.

These deep and lasting transformations are very important for allocators of capital like us. Secular trends are often associated with the opportunity for business development. It is in these times of change that innovations become new standards, and entrepreneurs who are able to identify these opportunities create value for the world and, as a consequence, wealth. As investors, we seek to partner with companies that create the future by capturing these trends.

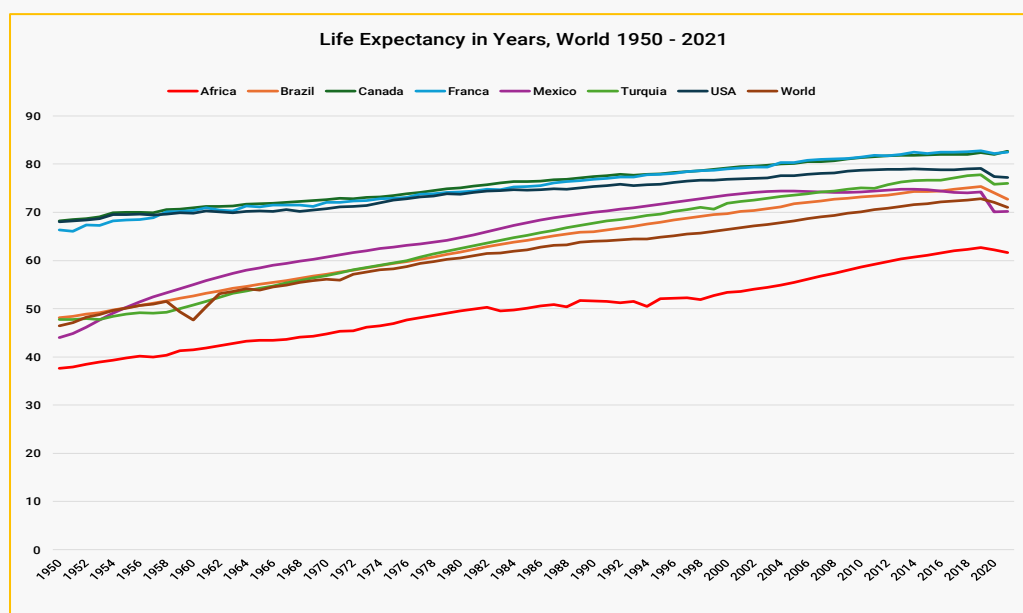
In recent years, scientific developments in the field of medical treatments have contributed to improving the living conditions of millions of people around the world – we cannot forget how quickly we were able to develop vaccines against Covid-19 in the 2020 pandemic. All this progress would not be possible without the innovative drive of scientists, doctors, governments and entrepreneurs dedicated to overcoming diseases and improving people's quality of life and longevity. And the results so far have been spectacular. We are very confident in what can still be achieved over the next few years.



2.3 The Great Discoveries in Medicine and Current Research Trends

Over the last century there has been an extraordinary development in medicine. From the smallpox vaccine – which was considered one of the great threats to humanity's existence at the end of the eighteenth century, killing approximately 10% of the planet's population at the time – to the discoveries of morphine in 1827, insulin in 1922, penicillin in 1942 and the polio vaccine in 1955, science has been able to offer effective answers and treatments for most major human diseases. As a result, we live in a time without historical precedent of improvement in the quality and life expectancy of people. According to the World Health Organization, life expectancy at birth in the world has risen from 46.5 years in 1950 to approximately 73 years in 2019 and is expected to reach 77 years in 2048. Unfortunately, the global data still hides relevant disparities in the different regions of the world. In 2019, life expectancy in Africa reached 62 years, a great improvement compared to 38 years in 1950, but still well below the life expectancy in Europe in 2019 of 78 years.

Behind this upward trend in life expectancy there is also an important epidemiological transition. With the advent of antibiotics, the success of vaccines in eradicating or near-eradicating infectious diseases such as smallpox and measles, the development of effective techniques for the treatment of other diseases such as tuberculosis and the improvement of public hygiene conditions, the vast majority of deaths in current times are a consequence of chronic diseases such as diabetes, cardiovascular diseases, cancer and Alzheimer's. According to the WHO, with the growth and aging of the global population "the world needs to intensify its efforts to find answers and treatments for chronic diseases". Therefore, much of the research budget has been directed towards the treatment of chronic diseases (NCDs). Over time, it has been observed that drugs based on chemical synthesis are incapable of being effective in the treatment of chronic diseases. Then, in the 1980s, research began on the so-called biological treatments, such as monoclonal antibodies, among others.



Source: Life Expectancy - Our World in Data



2.4 The Biological Drug Revolution

After the end of World War II, there was a pharmacological explosion and, consequently, the emergence of the American pharmaceutical industry, which inherited the spoils of the German pharmaceutical sector, with a focus on chemical synthesis. Small-molecule drugs are relatively simple chemical compounds, made up of 20 to 100 atoms, and have historically made up the majority of medical treatments. Such drugs are administered orally and due to their size and simplicity, they have a short shelf life and lack specifics, often leading to side effects. On the other hand, the simplicity and stable structure of small molecules leads to a relatively simple and inexpensive chemical manufacturing process that is easily standardized, and scalable. Aspirin is an example of a typical small molecule drug.

However, in the 1980s there was a revolution in drug production with the emergence of biologics – produced from a living organism, such as a virus, a bacterium or from our own cells. This new class of drugs has a much larger structure than smaller molecules, reaching about 5,000 to 50,000 atoms per molecule. The size of the large molecules makes them much more complex and unstable, and they are usually given by injection to prevent degradation by the gastrointestinal tract. The size of the molecule also prevents large molecules from penetrating cells, and because of this, they are highly specific molecules that target complex and difficult-to-treat diseases. This specificity creates a very effective treatment with fewer side effects. Given the size and complexity of large molecules, they have a much more complex and expensive manufacturing process, which requires many more inputs and high-performance instruments

to produce.

These new compounds have conquered a large space in the research of the pharmaceutical industry and have boosted the innovation portfolio and the arsenal of therapeutic compounds available. The top-selling drugs currently are Merck's Keytruda used in cancer treatment (US\$ 25 billion revenue in 2023), Pfizer's Corminaty (US\$ 15 billion in 2023), and AbbVie's Humira (US\$ 14 billion in 2023), all monoclonal antibodies targeted at treating cancer and autoimmune diseases.

The complexity of biologics requires a state-of-the-art production process, making the drugs very expensive, which prevents their use by a large portion of the population. However, we believe that in the near future, such drugs will be more affordable as production equipment technology advances and the production process becomes more efficient. In particular, it is worth mentioning the development of biosimilar drugs, which are synthetic versions of biologics, with a much lower production cost, which can be produced in a generic way as the patents of the respective biologics expire. Such advances will allow these new drugs to be accessible to everyone in the future.



2.5 How big is this market?

We consider it important to think about the pharmacology market from two different angles: the field of research with clinical studies, and the field of commercialization of approved drugs. Despite being highly linked activities, separating these two industry segments makes it easier to analyze the size of this market and the competitive environment.

As in other sectors such as information technology, as humanity has invested even more in the development of new drugs and vaccines, research techniques have become more sophisticated and technology in general has advanced, accelerating the discovery of new treatments in recent decades. Large companies established themselves in the sector and then the pharmaceutical industry as we know it today was formed, led by Pfizer, Merck, Roche, Amgen, GSK, Eli Lilly and others such as the notorious Novo Nordisk, currently in vogue due to the development of drugs based on GLP-1, such as Ozempic. This industry not only focused on research, but also allowed the massification of the production, and consequently, the distribution of these treatments to all of humanity.

2.5.1 Research

Research into new drugs and vaccines is an industry in itself, with many participants. In addition to pharmaceutical companies seeking new products for their portfolios, we still have many research initiatives organized within the public sector and universities. Therefore, mapping and aggregating the information on the

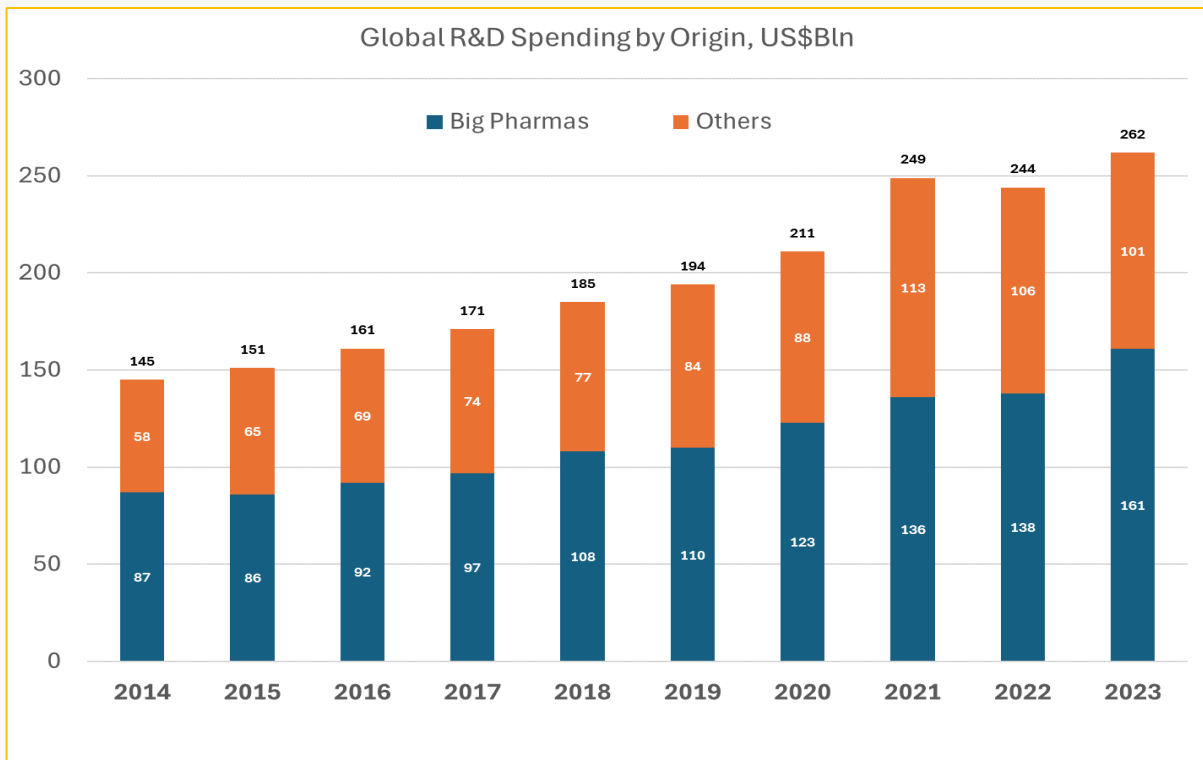
entire budget dedicated to drug research in the world can be a very complex task. However, we can assess the big numbers. Looking at big pharma where the information is public, the total budget reached US\$ 161 billion in 2023 according to IQVIA, 90% higher than in 2013, and representing approximately 23% of the sector's sales. Also considering governments, universities and private companies, the total budget dedicated to research in the world reached US\$ 260 billion at the end of last year.

In terms of composition, both the budget dedicated to research into new drugs based on small molecules and biologics has grown. However, the penetration of the latter has consistently increased as investment in the development of drugs focused on chronic diseases grows at a faster pace. This trend is expected to continue, based on recent successes and promising results, especially from Alzheimer's drugs.

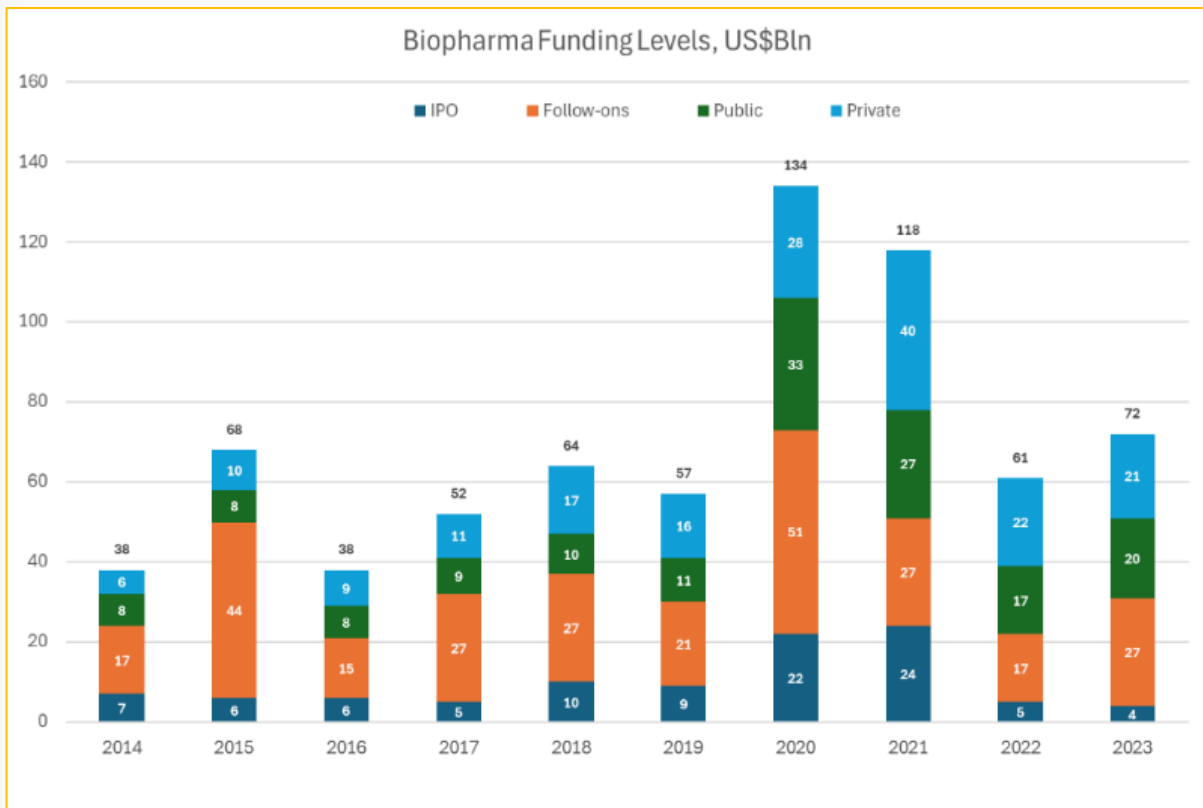
Finally, it is important to mention that, with the rise in interest rates in the US and the end of the pandemic, there was a significant drop in the levels of capital directed to biotechnology companies in the world in 2022 and 2023 compared to the volumes observed in 2020 and 2021, returning to the funding levels observed before the Covid-19 pandemic. For now, considering the increase in investment in research by large pharmaceutical companies, the scarcity of funding does not seem to have impacted the total amount allocated to research in the world.



2.5.1 Research



Source: Worldwide pharmaceutical R&D Spending 2014-2028, Statista



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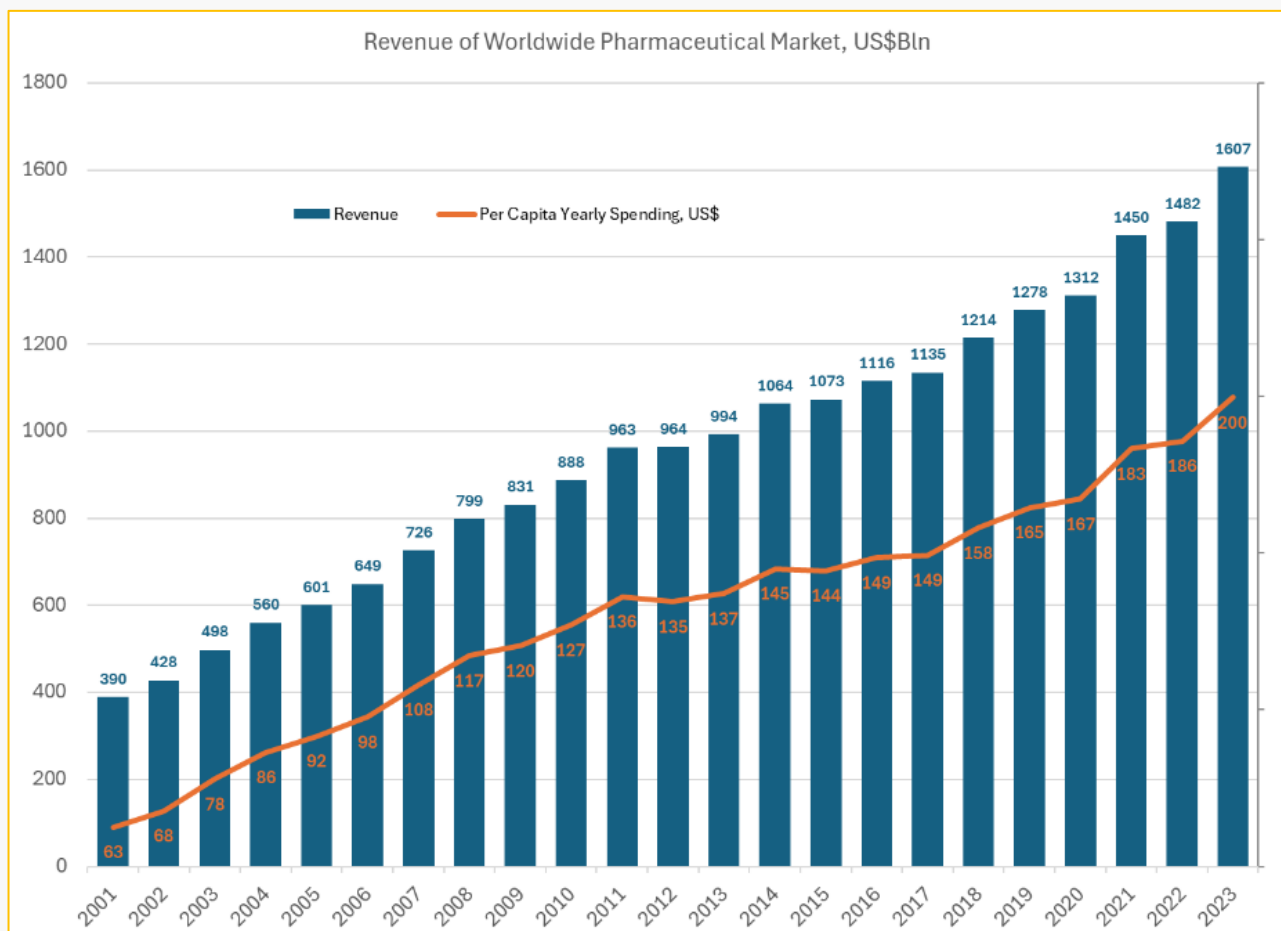


2.5.2 Commercialization

On the consumption side, total spending on medicines in the world reached US\$ 1.6 trillion in 2023, with an annualized growth of 5% over the past 10 years or 2.3% adjusted for inflation. It is possible that this rate will accelerate in the future. This acceleration depends on the success of the development of drugs with a great impact on the treatment of diseases, especially chronic diseases, as we have explained. Another factor influencing the size of this market going forward is the affordability of these treatments, which today are still extremely expensive and inaccessible to most people.

Logically, these are the big numbers and, within this industry, different areas have higher or lower growth. It is even possible to say that

we are experiencing a new cycle of discovery of new drugs in the treatment of chronic diseases based on new technologies. The growth of biological drugs in recent years has already been greater than that of the total market (10% p.a.), especially for cancer and diabetes drugs (GLP-1). We believe that this growth may accelerate as new technologies, such as mRNA and cell and gene therapy, mature. Although the first biological drugs appeared in the 1980s, we are still in the early stages of developing technologies such as gene therapy, which represents only 3% of the market for these drugs. We believe that as knowledge and research technology for these drugs advances, this growth can accelerate in the future.



Source: IQVIA – Global Medicine Spending and Usage Trends: Outlook 2024



2.6 Recent developments and what's to come

We are in a period of major investment in research that has been stimulated by the incredible potential of new technologies for producing medicines and humanity's need to deal with chronic diseases. In this context, the number of drugs in clinical trials worldwide has grown, as has the number of new drugs and treatments approved each year. To cite as an example, there are currently more than 1,500 clinical studies involving treatments with cell and gene therapies – of which, 60% seek treatments against various forms of cancer. New advances in the field of gene therapy promise to treat more than 7,000 genetic diseases, of which currently only 5% have any kind of treatment. The market expects this treatment modality to grow at a rate of ~30% per year in the coming years.

Another technology that has great potential is mRNA. The mRNA is like a messenger that carries information on how to make proteins from the DNA of our cells to the rest of the body. In gene therapy, scientists can tinker with this mRNA to send special instructions to cells, causing them to produce proteins that can correct problems or even attack diseases, such as cancer. The attractiveness of mRNA is that it is very versatile and quick to be adapted to new research and treatments. This has been made clear by how quickly COVID-19 vaccines have been developed using this technology. In the world of biotechnology, mRNA can be used to teach the cells of our immune system to recognize and destroy diseased cells. And unlike other approaches, mRNA usually doesn't stay permanently in our body, which means less risk of long-term side effects. Now, scientists are working to improve how this mRNA is delivered and kept stable in the body, opening the door to treatments for a range of diseases.

It is also worth mentioning here the anti-obesity drugs based on GLP-1 - a protein that treats type II diabetes and which, in 2023, received approval by the FDA for the treatment against obesity, and which has been widely used with enormous success. According to McKinsey, it is expected that by the end of the decade, more than 40% of the global population will be obese or overweight. The pharmaceutical companies currently responsible for these drugs, Eli Lilly and Novo Nordisk, are having a serious supply problem, as they are unable to keep up with the high demand for such drugs. Projections indicate that the GLP-1 market will reach US\$ 100 billion in revenue by the end of the decade.

Last but not least, we also saw in 2023 the approval of Leqembi, the first Alzheimer's drug, from the Japanese pharmaceutical company Eisai. Leqembi cannot repair cognitive damage, reverse the course of the disease, or prevent it from getting worse. But data from a large clinical trial suggest that the drug – given every two weeks as an intravenous infusion – may slow the decline by about five months over 18 months of treatment for people with mild symptoms. There are currently about 55 million people around the world diagnosed with Alzheimer's or dementia. This disease kills more people than breast and prostate cancer combined, and the number of deaths increased by 145% from 2000 to 2019.



2.7 In what way does the growth dynamics in the production and consumption of new drugs represent an investment opportunity? ?

One of the ways to capture returns associated with the upward trend in the consumption of drugs and vaccines in the world is to allocate capital to companies that are at the forefront of launching new drugs. A good example of this type of investment is the spectacular gains of Eli Lilly of +117% and Novo Nordisk of 58% in the last twelve months, due to the success of the anti-obesity drugs (Mounjaro, Ozempic and Wegovy). However, it is extremely difficult to predict which drugs will be successful in clinical trials. After all, the success rate from phase 1 of a clinical trial to FDA approval is only 10%. So we took a different approach. We believe that a good way to capture value in the pharmaceutical industry is not by betting on the next company that will be able to launch a blockbuster drug, but on its suppliers of equipment and inputs for the research and production of new drugs – the famous shovel sellers in the gold rush. In this context, we have two companies in our portfolio today – which in addition to being extraordinary from the point of view of their fundamentals, their business models, their competitive advantages, their culture and the people who manage them – benefit greatly from this secular trend: Danaher and Thermo Fisher.

Danaher is a family of Life Sciences and Diagnostics companies that has been increasing its exposure to the biologics market, which today already represents 30% of its revenue. In 2020, Danaher acquired GE's bioproduction arm for US\$ 20 billion – now under the name Cytiva – becoming the leading supplier of equipment and inputs to the biopharmaceutical industry. Its solutions are present in more than 90% of the monoclonal antibodies approved to date by the

FDA. Cytiva sells everything from bioreactors – huge tanks where cell culture takes place under specific conditions, to chromatography and filtration equipment, responsible for the purification stage of the molecule. Since this equipment is already installed in the customers' operation, Danaher sells the necessary inputs to operate such equipment, which guarantees it a very high level of recurring revenue. Once a drug is approved by the FDA, it is extremely difficult to change any component of the manufacturing, granting Danaher a lifetime contract with the drugmaker (until the drug's patent runs out). The more drugs that are produced, the more Danaher pays itself. In addition to growing revenue as demand for commercialized drugs increases, the company is extremely well positioned to capitalize on the potential development of new treatments, such as cell and gene therapy. In 2021, Danaher bought one of the world's largest plasmid DNA suppliers, a company called Aldevron, for US\$ 9.6 billion.

The ideal plasma DNA is the raw material for producing mRNA – which acts as a messenger that carries information on how to make proteins from the DNA of our cells to the rest of the body. In gene therapy, scientists can tinker with this mRNA to send special instructions to cells, causing them to produce proteins that can correct problems or even attack diseases, such as cancer. The attractiveness of mRNA is that it is very versatile and quick to be adapted to new research and treatments. This has been made clear by how quickly COVID-19 vaccines have been developed using this technology. In the world of biotechnology, mRNA can be used to teach the cells of our immune system to recognize and destroy diseased cells.



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Danaher is also a key partner in the development of Alzheimer's drugs, providing pharmaceutical companies with various inputs needed for production, such as reagents, cell culture, proteins, membranes, resins and filters. The demand for these drugs is estimated to drive the growth of the industry, which has historically been 15%.

Another investment we have that also captures value from the secular trend of increasing drug consumption through a different angle is Thermo Fisher. Thermo is also a company comprised of several Life Sciences and Diagnostics business lines, and is present in almost every sphere of activity in the industry, but with a somewhat different business portfolio than Danaher. It operates in the sector in several ways, from its distribution channel, through which it sells laboratory equipment, its own and third-party, to hospitals, academia and clinical laboratories – to its CDMO/CRO operation – contract development and manufacturing organization – where it acts as a partner of pharmaceutical companies and biotechs, being responsible for the production of drugs. In 2022, Moderna signed a contract with Thermo Fisher

to be responsible for producing the final "fill & finish" stage of Covid-19 vaccines. More recently, Novo Nordisk contracted with Thermo to be one of the commercial partners for the production of Ozempic. In addition, it is also worth mentioning its CRO arm – contract research organization – where it offers companies that are developing new drugs the service of implementing clinical studies and the approval of these new drugs with regulatory bodies such as the FDA.

Despite differing exposures within the industry, both companies benefit directly from the increased demand for new drugs, as well as benefit from all the capital that is reinvested in research and development, fostering new discoveries and breakthroughs for the future of medicine.



CONCLUSION

It's very inspiring to see all the progress we're making in medicine. We can already say that the development of this new generation of medicines that interact with the human body in a complex way and are capable of improving the quality of life of people affected by chronic diseases is another historic technological revolution for humanity. In addition, we consider all this value creation to be a great investment opportunity. Companies like Danaher and Thermo, which have businesses with deep competitive advantages, the highest quality executives, and a strategic position within the biotech industry, combine all the elements we look for in great deals. In particular, in addition to all the attributes of great companies, both have a fundamental participation in the progress of biological remedies and, consequently, dedicate themselves to a cause of the highest relevance to all of us.

Sincerely,
LUXOR INVESTIMENTOS

