



Fiera Apex: Our Approach to Biotech Investing

Healthcare remains one of the largest and fastest-growing sectors in the U.S. economy. We see the sector's prolific innovation, resilient demand, and support from long-term demographic trends and fundamentals as providing long-term drivers for continued growth.

National health expenditures are projected to continue outpacing average Gross Domestic Product (GDP) growth, accounting for 17.3% of the economy in 2022 and expected to reach 19.6% of GDP in 2031.¹ Driven by accelerating scientific discovery and innovation, combined with macro tailwinds, healthcare – and biopharma (i.e., biotechnology and pharmaceuticals) in particular – has emerged as one of the decade's most attractive and successful investment areas.

Since 2015, the proportion by market cap of biopharma names in the Russell 2500 Growth Index² has grown from 8% to almost 12% in 2024, making it one of the largest Industry groupings within the index. The increasing presence and outstanding returns makes ignoring biopharma increasingly difficult, particularly for active strategies benchmarked against the index. However,

the prevalence of binary outcomes in this industry provokes a need for a thoughtful approach to identifying investments and minimising risk. The Fiera Apex team’s investment process is attuned to navigate exactly this scenario, identifying the top-down secular trends providing tailwinds to growth in combination with bottom-up fundamental research to qualify buy candidates.

Key Secular Trends

A long runway for medical and technological innovation provides opportunities for durable, secular growth. The latest version of the International Statistical Classification of Diseases and Related Health Problems has about 85,000 listings.³ However, current

FDA-approved therapies address only a fraction of these conditions, reflecting a vast field of unmet medical needs. Looking ahead, we believe progress in drug discovery, diagnostics, devices, IT, and services will help improve prevention, identification, and treatment, while also resulting in lower costs wider access to care. Some themes we view as particularly key to strong secular growth include:

Solving unmet medical needs.

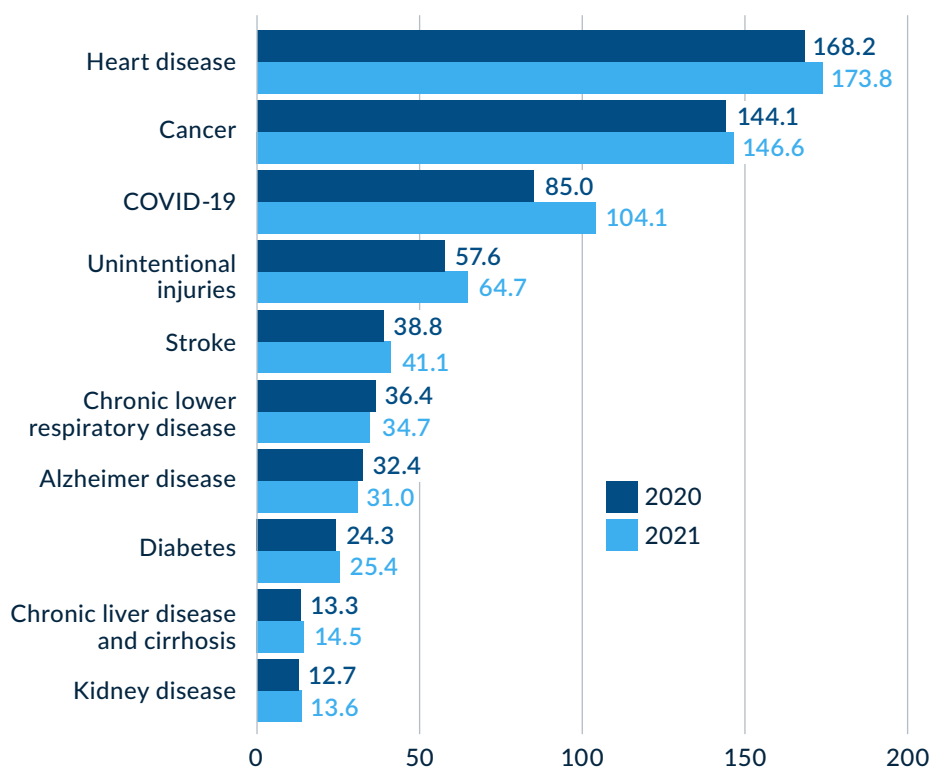
Molecular and protein therapeutics have provided solutions that have reined in epidemics, such as HIV and COVID-19, and transformed the course of chronic diseases, such as cystic fibrosis and rheumatoid arthritis, drastically improving and extending patients’ lives. Recently, newer modalities, such as cell and gene therapy, have cleared

roads to novel medicines with curative potential. Supported by the integration of genomic data and bioinformatics, we believe progress will continue to accelerate, with a strong likelihood of near-term breakthroughs of blockbuster potential across the spectrum of human health, from the leading causes of death (Chart 1), to the rarest orphan indications (Chart 2).

A demographic tailwind: healthcare demands will grow as the population skews older.

As the Baby Boomer generation ages into retirement, the proportion of people in the United States aged 65 and older is projected to increase from 17% in 2022 to about 22% in 2035.⁴ Meanwhile, Medicare spending is also expected to continue accelerating, reaching an average of 7.8% growth per year between 2025 and 2031, the fastest rate among the major payers.⁵

Chart 1: Leading Causes of Death Per 100,000 U.S. Standard Population



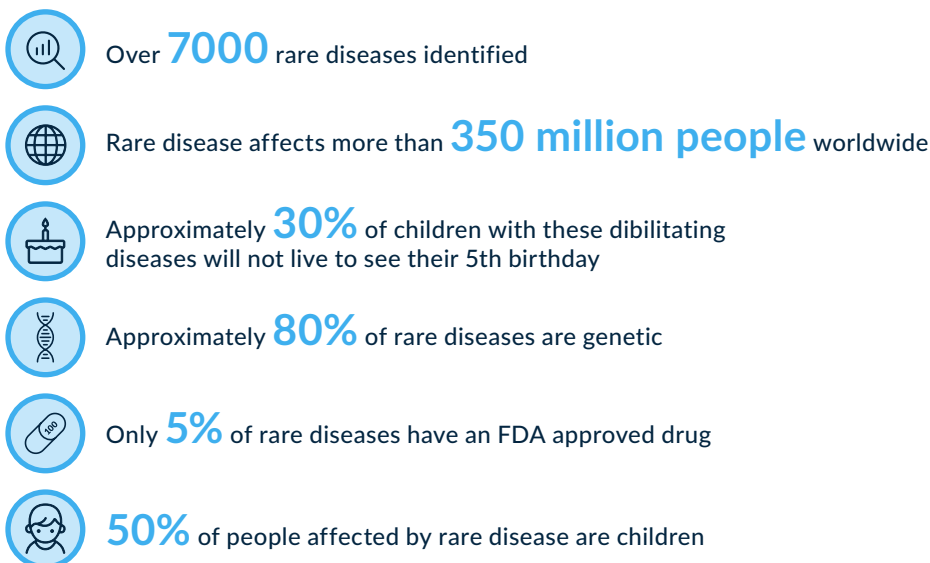
Source: NCHS, National Vital Statistics System, Mortality (December 2022). For more information please see the disclosures on the last page.

- Payer spending for polychronics (having >2 chronic conditions) is 5 times greater than those with no chronic conditions; 70% of people over the age of 65 are polychronic.⁶

Advances in health technology will support system efficiency, rein in costs, and increase access to care.

- With the cracking of the human genetic code, combined with evolving high-density data processing systems for testing and analysis, the surge in scientific progress has been – and should continue to be – exponential, propelling significant improvements across healthcare subsectors. Drug development has become faster and more precise, and the newer class of gene-based therapies have just begun to introduce some of the first potential cures for previously intractable conditions.

Chart 2: Orphan Diseases



Source: FDA, October 2017

- Life science technologies are integrating Artificial Intelligence and Machine Learning capabilities to process immense amounts of molecular and genomic data, paving the way to a deeper understanding of biology, better treatment decisions, and a new wave of medicines.
- Digital health and data could also drive a greater emphasis on preventative strategies to support healthy aging, as well as reduce inefficiencies and associated wasted costs that accumulate throughout the continuum of care.
- Additional opportunities exist in solutions to organise administrative and operative processes, as well as bring care to more people through remote monitoring and medical services.

The goal is early, accurate, and rapid disease identification in inexpensive and minimally invasive ways, while also determining some of the most successful routes of care, avoiding extra costs associated with misdiagnoses

and incorrect treatment decisions, and ultimately improving health.

Outlook For Biopharma

Biopharma’s positive fundamentals, bolstered by a constructive backdrop of innovation, regulatory tailwinds, and expanding access, should continue to fuel sector outperformance. Driven by rapid and dynamic advances in medicine and technology, we continue to view healthcare as holding some of the greatest potential for outsized returns. Current understanding of biology is just scratching the surface, and regulatory agencies are catching up with the speed of innovation, approving new medicines and technologies with increasing efficiency. Meanwhile, the complex payor environment is slowly becoming less burdened, bringing access to more people. Scientific breakthroughs have changed lives and facilitated dozens of multi-billion-dollar franchises and acquisitions. We believe innovation at

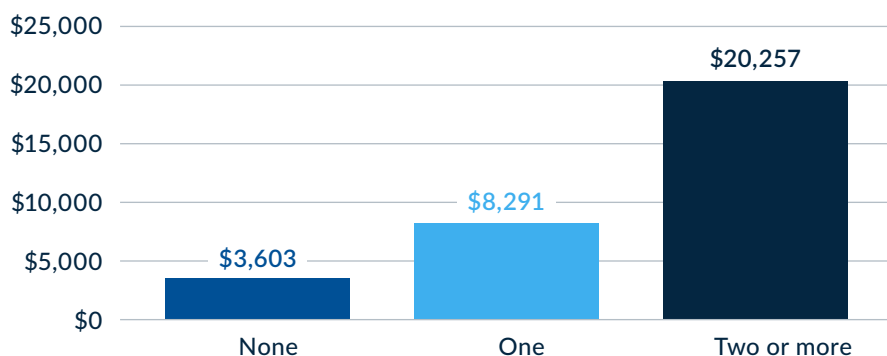
all levels will drive market returns and rotation into the sector for years to come.

We build our portfolio to participate in the growth of the industry while seeking to minimise downside risk.

Biopharma is largely an emerging growth industry, driven by powerful and persistent fundamental trends. However, we recognise the potential for risk when investing in the space. Across healthcare, we take a diversified approach, balancing emerging growth names, such as early biopharma companies, with stable growth names, including more mature and defensive companies across life science tools, technology, and services. From a bottom-up perspective, we believe a deep understanding of the science behind each company is key to unlocking investment insights and finding resilience and growth. We seek companies with some of the strongest science and durable competitive advantages, with businesses that solve problems in healthcare, whether by reducing costs, enhancing efficiency, and/or improving patient outcomes. We evaluate investment opportunities with vigorous, comprehensive research, conducting analysis at the scientific, financial, and market levels, as well as speaking to management teams and independent experts in the sector. Incorporating top-down research, we also assess macro



Spending Per Person by Number of Chronic Conditions



Source: HCCI 2017 Health Care Cost and Utilisation Report (February 2019)

drivers such as landscape evolution, policy updates, regulatory changes, and the capital markets environment, to assess overall probabilities of success.

Growth and good data remain undefeated. Following our thematic framework, we take a longer-term oriented investment approach, guided by catalyst-driven progress that withstands short-term market volatility. Industry growth within the index, as well as the outsized returns, create opportunities too big to miss, with potential alpha coming from strategic fundamental research, sector allocation, and stock selection.

Investment Example – Karuna Therapeutics

To evaluate the investment opportunity for Karuna Therapeutics, we performed a deep assessment of the company’s investigational assets and corresponding

market potential. Based in Boston and founded in 2009, Karuna focused on developing therapies to treat neurological disorders of high unmet need.

Assessing the science. We take a comprehensive approach to evaluating a company’s development platform, which we view as the foundation of a successful biopharma company. For any compound in development, we study the science behind it to determine how it works, what other effects it might have (e.g., potential interactions, off-target effects), and how successful it may be. Karuna’s lead asset, KarXT, was a novel, investigational medicine for schizophrenia, a disease that remains difficult to treat. Current drugs are only effective in some patients and only ameliorate psychosis (i.e., positive symptoms, such as delusions and hallucinations), while also coming with serious side effects such as weight gain, sedation, and cardiometabolic dysfunction. For our research, we

reviewed all available basic and clinical literature, including using chemical databases to study its molecular structure and scrutinising publications in scientific journals and conference presentations. Based on KarXT’s differentiated mechanism, we saw the potential for improved efficacy on positive symptoms, but also on negative symptoms (depression, apathy) and cognitive function (memory, attention), while maintaining a benign side effect profile. We spoke with independent experts to understand the unmet need and gain confidence on the commercial side. We concluded that KarXT was one of the highest quality, de-risked assets in the industry and was poised to become the key to unlocking indication and platform upside for the company.

Assessing the value. For smaller, pre-positive cash flow biopharma companies such as Karuna, we use an adjusted- Sum of the Parts analysis to determine the fair value of the stock. Based on extensive research and a detailed analysis of the competitive landscape, we built a forward-looking predictive model incorporating our estimates of the potential market size and the probabilities of success for each product. Milestones that the company would be expected to hit were clearly defined and tracked in order to validate our assumptions and thesis on an on-going basis.



Audrey Le, Ph.D.
Equity Analyst & Portfolio Manager

ENDNOTES

SOURCES ACCESSED FEBRUARY 2020

1. CMS Office of the Actuary
2. The Russell 2500™ Growth Index measures the performance of the small to mid-cap growth segment of the US equity universe.
3. World Health Organization
4. United States Census Bureau
5. Centers for Medicare
6. William Blair & Co.

uk.fieracapital.com

Important Disclosure

Fiera Capital Corporation (“**Fiera Capital**”) is a global independent asset management firm that delivers customized multi-asset solutions across public and private classes to institutional, financial intermediary and private wealth clients across North America, Europe and key markets in Asia and the Middle East. Fiera Capital trades under the ticker FSZ on the Toronto Stock Exchange. Fiera Capital does not provide investment advice to U.S. clients or offer investment advisory services in the US. In the US, asset management services are provided by Fiera Capital’s affiliates who are investment advisers that are registered with the U.S. Securities and Exchange Commission (the “SEC”) or exempt from registration. Registration with the SEC does not imply a certain level of skill or training. Each affiliated entity (each an “**Affiliate**”) of Fiera Capital only provides investment advisory or investment management services or offers investment funds in the jurisdictions where the Affiliate and/or the relevant product is registered or authorized to provide services pursuant to an exemption from registration.

This document is strictly confidential and for discussion purposes only. Its contents must not be disclosed or redistributed directly or indirectly, to any party other than the person to whom it has been delivered and that person’s professional advisers.

The information presented in this document, in whole or in part, is not investment, tax, legal or other advice, nor does it consider the investment objectives or financial circumstances of any investor.

Fiera Capital and its Affiliates reasonably believe that this document contains accurate information as at the date of publication; however, no representation is made that the information is accurate or complete and it may not be relied upon. Fiera Capital and its Affiliates will accept no liability arising from the use of this document.

Fiera Capital and its Affiliates do not make recommendations to buy or sell securities or investments in marketing materials. Dealing and/or advising services are only offered to qualified investors pursuant to applicable securities laws in each jurisdiction.

Past performance of any fund, strategy or investment is not an indication or guarantee of future results. Performance information assumes the reinvestment of all investment income and distributions and does not account for any fees or income taxes paid by the investor. All investments have the potential for loss. Target returns are forward-looking, do not represent actual performance, there is no guarantee that such performance will be achieved, and actual results may vary substantially.

This document may contain “forward-looking statements” which reflect the current expectations of Fiera Capital and/or its Affiliates. These statements reflect current beliefs, expectations and assumptions with respect to future events and are based on information currently available. Although based upon what Fiera Capital and its affiliates believe to be reasonable assumptions, there is no guarantee that actual results, performance, or achievements will be consistent with these forward-looking statements. There is no obligation for Fiera Capital and/or its Affiliates to update or alter any forward-looking statements, whether as a result of new information, future events or otherwise.

Strategy data such as ratios and other measures which may be presented herein are for reference only and may be used by prospective investors to evaluate and compare the strategy. Other metrics are available and should be considered prior to investment as those provided herein are the subjective choice of the manager. The weighting of such subjective factors in a different manner would likely lead to different conclusions.

Strategy details, including holdings and exposure data, as well as other characteristics, are as of the date noted and subject to change. Specific holdings identified are not representative of all holdings and it should not be assumed that the holdings identified were or will be profitable.

Certain fund or strategy performance and characteristics may be compared with those of well-known and widely recognized indices. Holdings may differ significantly from the securities that comprise the representative index. It is not possible to invest directly in an index. Investors pursuing a strategy like an index may experience higher or lower returns and will bear the cost of fees and expenses that will reduce returns, whereas an index does not. Generally, an index that is used to compare performance of a fund or strategy, as applicable, is the closest aligned regarding composition, volatility, or other factors.

Every investment is subject to various risks and such risks should be carefully considered by prospective investors before they make any investment decision. No investment strategy or risk management technique can guarantee returns or eliminate risk in every market environment. Each investor should read all related constating documents and/or consult their own advisors as to legal, tax, accounting, regulatory, and related matters prior to making an investment.

The ESG or impact goals, commitments, incentives and initiatives outlined in this document are purely voluntary, may have limited impact on investment decisions and/or the management of investments and do not constitute a guarantee, promise or commitment regarding actual or potential positive impacts or outcomes associated

with investments made by funds managed by the firm. The firm has established, and may in the future establish, certain ESG or impact goals, commitments, incentives and initiatives, including but not limited to those relating to diversity, equity and inclusion and greenhouse gas emissions reductions. Any ESG or impact goals, commitments, incentives and initiatives referenced in any information, reporting or disclosures published by the firm are not being promoted and do not bind any investment decisions made in respect of, or stewardship of, any funds managed by the firm for the purposes of Article 8 of Regulation (EU) 2019/2088 on sustainability-related disclosures, in the financial services sector. Any measures implemented in respect of such ESG or impact goals, commitments, incentives and initiatives may not be immediately applicable to the investments of any funds managed by the firm and any implementation can be overridden or ignored at the sole discretion of the firm. There can be no assurance that ESG policies and procedures as described herein, including policies and procedures related to responsible investment or the application of ESG-related criteria or reviews to the investment process will continue; such policies and procedures could change, even materially, or may not be applied to a particular investment.

The following risks may be inherent in the funds and strategies mentioned on these pages.

Equity risk: value of stock may decline rapidly and can remain low indefinitely. **Market risk:** the market value of a security may move up or down based upon a change in market or economic conditions. **Liquidity risk:** the strategy may be unable to find a buyer for its investments when it seeks to sell them. **General risk:** any investment that has the possibility for profits also has the possibility of losses, including loss of principal. **ESG and Sustainability risk** may result in a material negative impact on the value of an investment and performance of the portfolio. **Geographic concentration risk** may result in performance being more strongly affected by any conditions affecting those countries or regions in which the portfolio's assets are concentrated. **Investment portfolio risk:** investing in portfolios involves certain risks an investor would not face if investing in markets directly. **Operational risk** may cause losses as a result of incidents caused by people, systems, and/or processes. **Projections and Market Conditions:** We may rely upon projections developed by the investment manager or a portfolio entity concerning a portfolio investment's future performance. Projections are inherently subject to uncertainty and factors beyond the control of the manager and the portfolio entity. **Regulation:** The manager's operations may be subject to extensive general and industry specific laws and regulations. Private strategies are not subject to the same regulatory requirements as registered strategies. **No Market:** The LP Units are being sold on a private placement basis in reliance on exemptions from prospectus and registration requirements of applicable securities laws and are subject to restrictions on transfer thereunder. Please refer to the Confidential Private Placement Memorandum for additional information on the risks inherent in the funds and strategies mentioned herein. **Meteorological and Force Majeure Events Risk:** Certain infrastructure assets are dependent on meteorological and atmospheric conditions or may be subject to catastrophic events and other events of force majeure. **Weather:** Weather represents a significant operating risk affecting the agriculture and forestry industry. **Commodity prices:** Cash flow and operating results of the strategy are highly dependent on agricultural commodity prices which can be expected to fluctuate significantly over time. **Water:** Water is of primary importance to agricultural production. **Third Party Risk:** The financial returns may be adversely affected by the reliance on third party partners or a counterparty's default.

For further risks we refer to the relevant fund prospectus.

United Kingdom: This document is issued by Fiera Capital (UK) Limited, an affiliate of Fiera Capital Corporation. Fiera Capital (UK) Limited is authorized and regulated by the Financial Conduct Authority and is registered with the US Securities and Exchange Commission ("SEC") as investment adviser. Registration with the SEC does not imply a certain level of skill or training.

Abu Dhabi Global Markets: This document is issued by Fiera Capital (UK) Limited, an affiliate of Fiera Capital Corporation. Fiera Capital (UK) Limited is regulated by the Financial Services Regulatory Authority.

United Kingdom – Fiera Real Estate UK: This document is issued by Fiera Real Estate Investors UK Limited, an affiliate of Fiera Capital Corporation. Fiera Real Estate Investors UK Limited is authorized and regulated by the Financial Conduct Authority.

European Economic Area (EEA): This document is issued by Fiera Capital (Germany) GmbH ("**Fiera Germany**"), an affiliate of Fiera Capital Corporation. Fiera Germany is authorized and regulated by the Bundesanstalt für Finanzdienstleistungsaufsicht (BaFin).

United States: This document is issued by Fiera Capital Inc. ("**Fiera U.S.A.**"), an affiliate of Fiera Capital Corporation. Fiera U.S.A. is an investment adviser based in New York City registered with the Securities and Exchange Commission ("SEC"). Registration with the SEC does not imply a certain level of skill or training.

United States - Fiera Infrastructure: This document is issued by Fiera Infrastructure Inc. ("**Fiera Infrastructure**"), an affiliate of Fiera Capital Corporation. Fiera Infrastructure is registered as an exempt reporting adviser with the Securities and Exchange Commission ("SEC"). Registration with the SEC does not imply a certain level of skill or training.

United States - Fiera Comox: This document is issued by Fiera Comox Partners Inc. ("**Fiera Comox**"), an affiliate of Fiera Capital Corporation. Fiera Comox is registered as an investment adviser with the Securities and Exchange Commission ("SEC"). Registration with the SEC does not imply a certain level of skill or training.

Canada

Fiera Real Estate Investments Limited ("Fiera Real Estate**")**, a wholly owned subsidiary of Fiera Capital Corporation is an investment manager of real estate through a range of investments funds.

Fiera Infrastructure Inc. ("Fiera Infra**")**, a subsidiary of Fiera Capital Corporation is a leading global mid-market direct infrastructure investor operating across all subsectors of the infrastructure asset class.

Fiera Comox Partners Inc. ("Fiera Comox**")**, a subsidiary of Fiera Capital Corporation is a global investment manager that manages private alternative strategies in Private Credit, Agriculture, Private Equity and Timberland.

Fiera Private Debt Inc. ("Fiera Private Debt**")**, a subsidiary of Fiera Capital Corporation provides innovative investment solutions to a wide range of investors through two distinct private debt strategies: corporate debt and infrastructure debt.

Please find an overview of registrations of Fiera Capital Corporation and certain of its subsidiaries here: <https://www.fieracapital.com/en/registrations-and-exemptions>.

Version STRENG002