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Biotechnology Industry Study

Final Report

Securing America's Future in Biotechnology

The Dwight D. Eisenhower School for National Security and Resource Strategy
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ABSTRACT

The United States (U.S.) is currently the global leader in the human health segment of biotechnology. However, China, Russia, and other countries are also devoting significant resources to compete in the biotechnology industry. In an era of Great Power Competition, where nations are vying for power and influence, economic and national security requires a holistic, balanced, and sustainable strategy. The U.S. must set conditions for success to remain the leader and mature an ethical and innovative biotechnology ecosystem, fortifying all instruments of national power. The U.S. must set the conditions for success to remain the leader in biotechnology. Future human health, economic growth, and national security will depend on governments, academia, and industry taking the proper steps to grow a thriving and ethical biotechnology industry while making strategic investments to maintain primacy against peer competitors such as China. The U.S. must proactively invest in human capital, government enablement, and other foundational components of the biotechnology ecosystem to secure its competitive advantage and remain ahead of its rivals in biotechnology. The recommendations contained in this paper will benefit the entire economy and the DoD in particular.

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EXECUTIVE SUMMARY

Biotechnology is the use of "biology to harness cellular and biomolecular processes to develop technologies and products that help improve lives and the health of our planet."[1] The biotechnology industry is a highly competitive global industry with substantial national security and economic implications. The U.S. is currently the global leader in biotechnology, but China, Russia, and other countries are also devoting significant resources to overtake the U.S.'s dominant position.

Sustaining biotechnology innovation is integral to economic and national security. The triumph of the U.S.'s biotechnology industry during the COVID-19 pandemic, producing two highly effective vaccines using entirely new technology with messenger RNA, and in record time, shows that the U.S.'s competitive edge in biotechnology remains largely intact. In an era of Great Power Competition, where nations are vying for power and influence, economic and national security requires a holistic, balanced, and sustainable strategy. The U.S. must set conditions for success to remain the leader and mature an ethical and innovative biotechnology ecosystem, fortifying all instruments of national power.

As the above definition implies, biotechnology is a set of multiple industries, all deriving from the use of biological molecules to create products, services, and systems. This paper focuses on the human health technologies industry segment as it currently represents 56% of the global biotechnology industry. Biotechnology innovation relies on more than just funding. It requires a thriving ecosystem of industry, academia, skilled workers, partnerships, culture, and policy to drive innovation. While the current U.S. ecosystem demonstrates strengths and has delivered essential benefits, the future biotechnology ecosystem must nonetheless be able to respond more quickly than it did with COVID-19. Imagine a virus as deadly as Ebola spreading as fast as COVID-19. The global community must rely on advances in biotechnology to respond to other threats that do not respect borders, such as climate change, population displacement, and aging populations where diseases bring high costs for prevention and treatment.

This paper assesses the strategic environment and evaluates strengths, weaknesses, opportunities, and threats to identify gaps compared to near-peer competitors. It considers Chinese and Russian strategies and determines where the U.S. needs to be in the future. Finally, it suggests policy recommendations and strategic investments to close any gaps to keep the U.S. innovating and leading in biotechnology. The U.S. must proactively invest in human capital, government enablement, and other foundational components of the biotechnology ecosystem to secure its competitive advantage and remain ahead of its rivals in biotechnology. The right investments in all three components will drive the U.S. biotechnology ecosystem toward game-changing technologies and innovations. The recommendations contained in this paper will benefit the entire economy and the DoD in particular.

INTRODUCTION

Biotechnology puts humans at the forefront of a new synthetic age that can help solve significant global problems, as demonstrated during the current COVID-19 pandemic. Biotechnology is composed of dual-use technologies that bring both opportunities and threats to health, prosperity, and national security. The biotechnology industry includes the human health, industrial, animal health, agriculture, environmental, and other technology product and service segments, as seen in the IBIS*World* Global Biotechnology Industry Report below.[2]

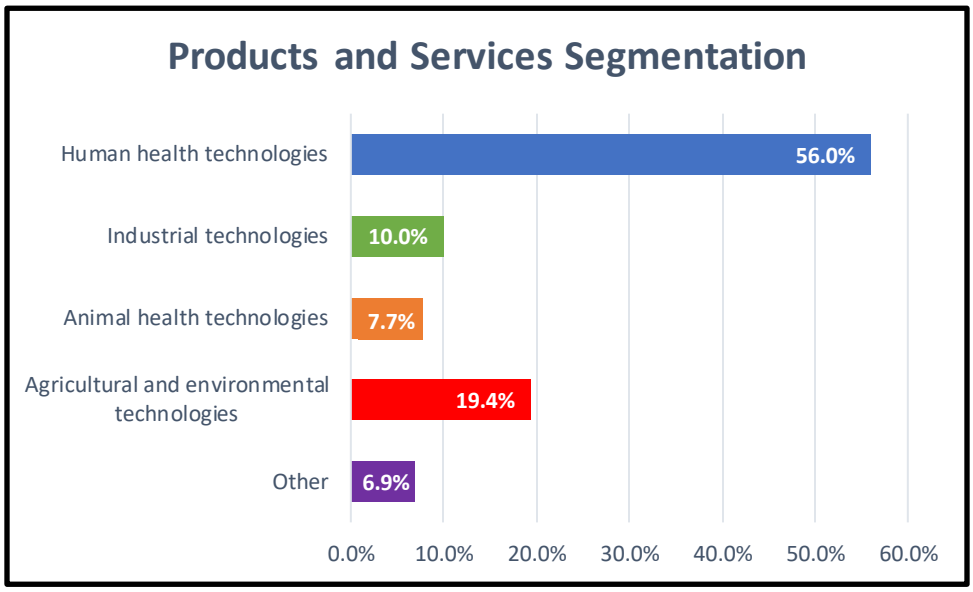


Figure 1: IBIS*World* Global Biotechnology Industry Report[3]

The Eisenhower School AY 20-21 Biotechnology Industry Study focuses on human health technologies, which in 2019 accounted for more than half of industry revenue. It examines why biotechnology is important by evaluating current conditions and significant factors necessary to chart a path toward securing U.S. biotechnology leadership and innovation.

The U.S. must maintain its dominant position in human health technologies. U.S. economic and national security will depend on government, academia, and industry taking steps to grow a thriving and ethical industry while making collective and strategic investments to remain ahead of peer competitors such as China. Because of implications to the health of the population and the economy's strength, which is fundamental to resourcing all instruments of power, biotechnology is vital to U.S. national security in general and to DoD in particular. The following recommendations demonstrate ways the U.S. can prioritize and invest in human capital, government enablement, and the other foundational components to remain ahead of rivals in human health technologies. The U.S. should:

1. Establish the Office of Science and Technology Policy as a permanent cabinet-level position and define its roles and authority.
2. Simplify grant processes, so academia stimulates science, technology, engineering, and math (STEM) youth engagement to fill STEM pipelines.
3. Change student visas to allow accompanied temporary residency during STEM education and issue a work visa or permanent resident card upon graduation. The STEM pipeline includes international students that must depart within 60 days of graduation.

4. Increase federal funding of research to at least one percent of gross domestic product to preserve the U.S. lead in human health technologies prioritizing basic research.
5. Lead a global cooperative effort to update international trade agreements and World Trade Organization standards and intellectual property rights and data policies. Existing agreements and global standards do not align with current industry practices.
6. Incentivize the synthetic biological production of critical active pharmaceutical ingredients (API) through short-term qualifying research expenditure tax credits to diversify risk and reduce foreign dependency.
7. Incentivize private firms to establish broadband internet capabilities of at least 800-megabit download / 800-megabit upload capability.

IMPORTANCE AND STAKEHOLDER INTERESTS

According to the National Defense Strategy, biotechnology is one of the "very technologies that ensure we will be able to fight and win the wars for the future."[4] Supporting the warfighter is an essential reason to remain a leader in human health technologies.

In addition, the National Biodefense Strategy clearly states that "as the biological threat continues to evolve, so must our biodefense capabilities. Furthermore, in 2016, the President's Council of Advisors on Science and Technology (PCAST) described a "new landscape" of biological and biotechnological threats to the U.S.[5] The council cautioned the U.S. President that the billions of dollars spent on biodefense since 2001 were insufficient to meet these challenges.

The U.S. cannot win wars without a healthy population and a strong economy powered by thriving industries. Of the various possible threats to the U.S., none provides a greater example than the far-reaching death and destruction wrought by the COVID-19 pandemic. Additionally, the U.S. must recognize the possibility of synthetic pathogens engineered to disrupt human health and the economy. By coordinating programs, actions, and budgets, the federal government can better anticipate, prevent, prepare for, respond to, and recover from biological disasters."[6] This makes the U.S. and global populations as well as DoD and the warfighter key stakeholders in human health technologies.

U.S. national security derives benefits from biotechnology, including improvements to the population's health, productivity, and cost-savings derived from advancements in disease prevention (e.g., vaccine-preventable illnesses), early diagnosis and management of chronic diseases (e.g., diabetes mellitus, hypertension, hyperlipidemia), curative cancer treatments, and especially lower pharmaceutical costs. From advanced diagnostics and small-molecule pharmaceuticals to a greater understanding (and manipulation) of the human genome, biotechnology continually offers new pathways to improving health and performance.

The Human Genome Project (HGP) is one of the most successful examples of innovative government biotechnology projects in recent history. The project exemplifies the power, necessity, and success of extensive, integrated, international, and cross-disciplinary efforts directed towards major, complex objectives. Support and funding from the Department of Energy, the National Institutes of Health, and later the UK's Medical Research Council and Wellcome Trust funded the HGP and enabled it to run on a vast scale. The labs from these organizations then joined with collaborators across six countries to accomplish the massive task of sequencing the first human genome. HGP is directly responsible for the success of COVID-19 vaccines. Thanks to the technology that made HGP possible, it is now trivial to sequence any given virus. Scientists were able to determine quickly what kind of virus it was and what approach was necessary to go after it, thanks to HGP technology. After the Chinese lab released the sequence in January 2020, a process that takes one or two hours in a good lab allowed

scientists worldwide to begin researching the virus without needing a sample. The first vaccine design was made possible within the first 24 hours. The computing power and technology developed to assemble the complete three billion-letter human genome sequence from countless fragments are now being used to follow tiny changes in the viral genome as it spreads. This gives the industry an enormous ability to track the virus, watch the virus's evolution, and develop treatments and vaccines for future variants. In addition to the health benefits still evolving, the economics are almost as impressive. A $3 billion investment generated "$965 billion in economic output between 1988 and 2012, creating more than $293 billion in personal income through wages and benefits and nearly 4 million jobs."[7] The HGP is a powerful example of the triple helix (academia, industry, and government) coordination and federal funding of basic research that is still leading to profound scientific and human health innovations decades later.

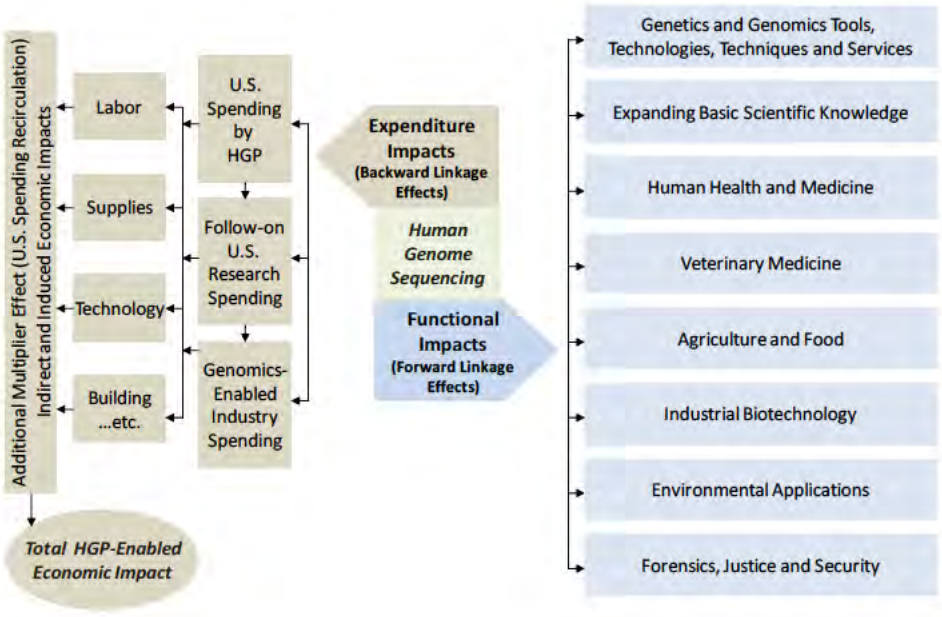


Figure 2: Human Genome Project Economic Link to Functional Impacts[8]

American leadership in this industry is imperative to U.S. national security. However, China is also striving to emerge as the global leader of emerging technologies, including human health technologies, to drive the Chinese economy and unlock the many dual-use military applications. While further behind, Russia has also identified biotechnology as a national priority.

STRATEGIC ANALYSIS

Humans have used biotechnology since the dawn of civilization. However, it wasn't until the early 20th century that biotechnology appeared in the human conscience. In 1919, Hungarian engineer Karl Ereky coined the term "biotechnology" to describe the production of materials from biological processes. The first U.S. biotechnology patent, for a technique for recombinant DNA, was submitted in 1974 but was not awarded until 1980. The gene-splicing method, called the Cohen-Boyer method, revolutionized biological research and launched the multi-billion-dollar biotechnology industry. Since that time, the U.S. biotechnology industry has held a leading position as an economic and innovation driver and engine of job growth.

The global biotechnology industry is large and growing. The U.S. accounts for half of the industry revenues, followed by Asia-Pacific and Europe. As many industries struggled during the challenges caused by COVID-19, human health technologies and the biotechnology industry benefited. Globally, the highly competitive biotechnology industry expects to rise to a $2.4 trillion industry as soon as 2028, with significant human life expectancies and age-related illnesses increasing the demand for medicines and new treatments.[9] In addition, advancements such as those discussed described below (trends shaping the U.S. biotechnology industry) will propel market growth in the industry. As a result, the pressure to innovate to respond to demand creates opportunities that draw new entrants into the biotechnology sector. Between 2019 and 2020, the industry saw double-digit growth in fundraising from venture capital, partnerships, co-developments.[10]

Currently, the U.S. and Europe lead the biotechnology industry in terms of R&D investments (public and private). U.S. R&D spend stood at a little more than three percent of GDP in 2019, and life sciences saw a surge of 22% from 2018 to 2019 in R&D spending. In Europe, biotechnology is significant, accounting for an estimated 23.6% of the global biotechnology industry establishments in 2019."[11] Combined, the U.S. and Europe created over 50% of the worldwide biotechnology establishments in 2019. Attaining the label "booming," China's biotechnology industry achieved a market value of $19B in 2019 with China's pharmaceutical market—the second largest market globally after the U.S., representing 98% of China's overall biotechnology market that year. Russia's biotechnology market had the largest revenue in its pharmaceutical sector in 2019, measured at $1.5B,[12] a successful by-product of the evolving progress of the country's "Pharma 2020" strategy.

On average, it generally takes over ten years and costs $2.6 billion to bring a drug to market. However, there are four expedited processes (breakthrough therapy, fast track, accelerated approval, and priority review) for serious diseases or unmet medical needs. The expedited processes can cut the process by up to 3.2 years. Further, the U.S. anticipates new growth drivers, such as the U.S. government's emphasis on biotechnology's role in pandemic prevention and response, onshoring trends, and rapid expansion of bio-manufacturing to shape the industry forward. The following sections look at the critical factors underpinning the U.S. biotechnology sector.

Trends Shaping the U.S. Biotechnology Industry in 2021 and Beyond

With constant research and technology improvements underpinning biotechnology scientific discoveries, the breakthroughs below will continue to shape the industry in the decades ahead:

Genetics: As a central pillar of biology, the field of genetics overlaps with biotechnology, medicine, and agriculture. Thanks to advancements in this arena, healthcare delivery can be personalized and customized based on human DNA, paving the way for personalized diagnostics and treatment of diseases.

Increased Stakeholder Collaboration: Innovation drives life sciences' discoveries that result from collaboration among government, academia and companies, large and small. The relationship among these stakeholders is generally referred to as the triple helix and will be discussed in more detail in the next section. Cloud computing will enable all stakeholders to share information and collaborate in real-time across borders, potentially opening research to

larger groups of players, lowering barriers to entry, and incentivizing stakeholders to stay in the game.

Smart Technologies: Next-generation computing technologies such as machine learning and artificial intelligence (AI) will improve efficiencies in the manufacturing of new products and the diagnosis and treatment of diseases. Smart technologies such as additive manufacturing, robotics, and wearables represent immense opportunities for U.S. companies to enhance their competitive advantage in the global market.

Value-Based Pricing Models: The model expects to tie the pricing of medicines to their effectiveness in treating illnesses efficiently and cost effectively. As a result, it expects value-based pricing contracts to align the incentives of manufacturers and buyers of medicines and medical products, enhancing the bargaining power of purchasers,[13] potentially reducing industry profitability. While there are benefits in the alignment of consumers' interests and those of manufacturers, value-based pricing systems, combined with other inputs such as patents and the high cost of R&D to produce exciting new medicines, can potentially exert downward pressure on R&D spending and innovation.

Synthetic Biology ("SynBio"): By 2030, most Americans will probably have eaten, worn, or used a product created using synthetic biology. Researchers harness the power of natural organisms to engineer solutions to real-world challenges, such as eradicating malaria, treating chronic diseases, reducing greenhouse emissions, and securing the resiliency of crops. As positive applications of SynBio are expected to grow, so too will the concern of SynBio as a biosecurity risk and potential bioterrorism tool.[14]

Human Health Technologies Ecosystem and Triple Helix

Human health technologies' growth and development will result from the interaction of the triple helix in an ecosystem. The triple helix fosters relationships that most effectively transition scientific breakthroughs created by research into developing usable products produced by industry. These triple helix relationships are a vital component of the larger biotechnology ecosystem. An ecosystem defined by *Britannica* "is the complex of living organisms, their physical environment, and all their interrelationships in a particular unit of space."[15] Ecosystem is an apt word to describe the dynamic non-linear, sometimes competing and sometimes cooperating stakeholder relationships, laws, policies, and infrastructure that influence the biotechnology and human health technologies.

Triple Helix

The triple helix represents the interplay between three stakeholders: academia, industry, and government.[16] The role of the triple helix is to help these stakeholders move from basic research to the final delivery of a product or service (i.e., go from research to development) as efficiently as possible. Human health technologies rely on innovative collaboration as modeled by the triple helix as seen in Figure 3.

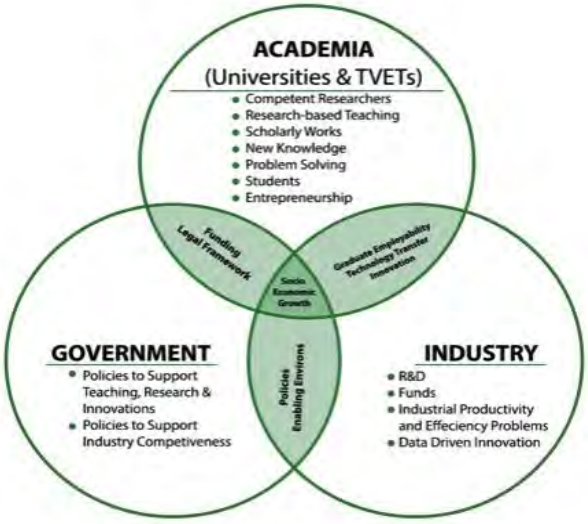


Figure 3: Triple Helix Model[17]

Academia (including universities, two-year colleges, and technical and vocational education institutions) provides the expertise, labor force, and much of the basic research discoveries that transition to industry for commercialization. Academic research is primarily funded by federal research dollars, but collaborations with industry are providing new avenues for funding and moving a discovery through the various phases to obtain market approval. Government manages the operational framework through regulations, intellectual property protection, and some financial support (other financial support comes from companies and private entities) to academia and industry. Industry also provides some basic research, develops goods and services, and translates the research into products and delivers them into the market. Each of the intersections provides additional capability and interaction. Government intersection with academia provides additional necessary research opportunities, while intersection with industry provides government-specific applications and regulations and policies that support industry and academic efforts (intellectual property protection, trade policies, etc.). The academic and industrial intersection provides transfer capability from basic to applied research and transformation to a market-ready product.[18 19 20]

The triple helix is essential to general innovation and is a key component of the biotechnology industry. Triple helix hubs have developed domestically and abroad to support the industry. North American biotechnology triple helix sites include Boston, Philadelphia, Los Angeles, and Silicon Valley. These areas are described and function as clusters, as shown in Figure 4.[21]

Figure 4: Global Startup Hubs: Biotechnology[22]

Academia

To continue with the framework, academia produces much of the research that transitions to industry for commercialization. In biotechnology, academia plays a significant role in generating meaningful accomplishments in biomedical research. As an integral player in the triple helix, American innovation is driven partly by academic research, which provides both the labor force and basic scientific knowledge. Federal research dollars largely fund academic research to fuel the innovation system.

Human Health Technologies Industry

The human health technology industry's role in the triple helix model is to take the successes from basic research and develop them into useable products. In the industry, companies range from start-ups to more well-established companies. Companies can fund the transition by making profits, meaning their return on invested capital (ROIC) is greater than their weighted average cost of capital (WACC). When ROIC is greater than WACC, a company is creating value. This value can then be funneled back to fund more research to continue the cycle of research, development, sales, and profit. These companies have multiple sources of funds: retained earnings, new direct investment via new issuances of stocks and bonds sold into the financial markets. However, until a company is solvent enough to operate at a level with their ROIC greater than WACC, the company must find funding from outside the company.

The established firms utilize proceeds from previous sales to conduct product development from basic research. The lack of funding may stymy product development, resulting in the valley of death concept. The valley of death is when a product fails to transform from research to product from lack of funding. Like the Small Business Innovation Research and Small Business Technology Transfer programs, venture capital firms and government support provide the necessary capital to fund product development. Without these funds, the valley of death constrains innovation to scientific research.[23]

Porter's Five Forces provides a framework for describing and understanding drivers in the biotechnology industry. Figure 5 summarizes Porter's Five Forces in biotechnology.[24]

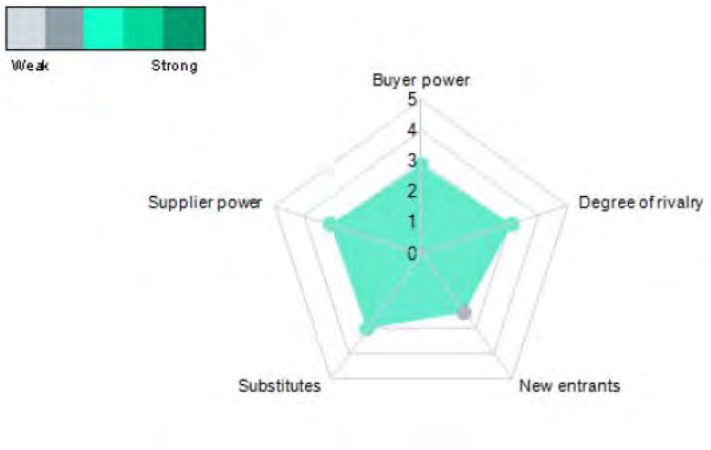


Figure 5: Porter's Five Forces Summary

Buyer Power: This is the strongest force in the human health technologies industry. Though government healthcare providers and managed care organizations concentrate buying power in biotechnology, lack of valid substitutes and demand for life-saving treatments reduces downward pressure on prices. The U.S. patent system prevents competitors from providing duplicate products during the term of the patent. As the U.S.' population ages, more demand for end-of-life care further decreases buyer power. Figure 6 summarizes buyer power in biotechnology.[25]

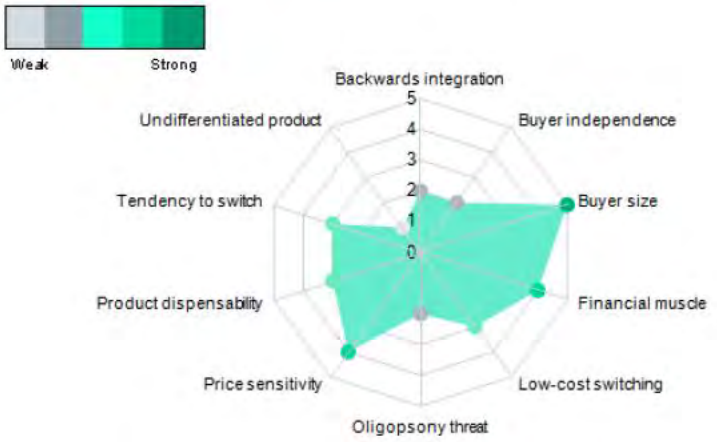


Figure 6: Buyer Power

Supplier Power: Inputs in biotechnology include lab equipment, production equipment, raw material, and labor. Due to the lack of differentiation between lab equipment suppliers, they lack power against biotechnology firms. Due to the specialization of suppliers for key ingredients or a limited number of approved sources, suppliers may find increased power against firms. Firms can offset this by producing their own key ingredients. The bargaining power of suppliers, thus, is moderate to high. Barriers to international trade also tend to increase supplier power.

Labor in this industry is dependent on STEM workers. Figure 7 summarizes supplier power in biotechnology.[26]

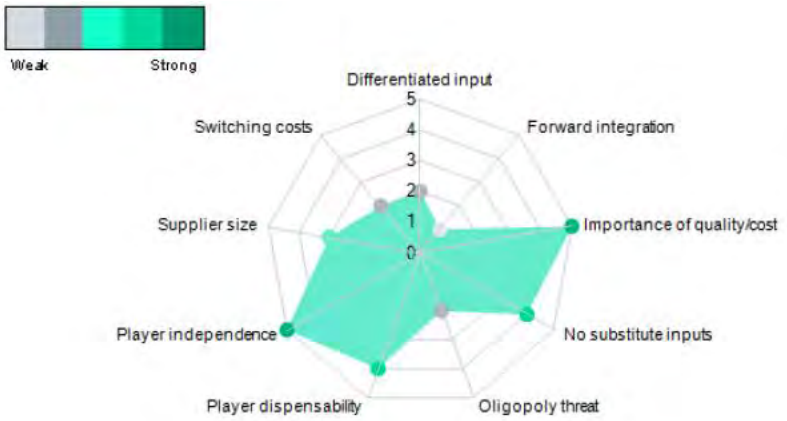


Figure 7: Supplier Power

New Entrants: The threat of new entrants in this sector can be considered low to moderate. Substantial intellectual property rights and a healthcare market largely without government-regulated pricing in the U.S. attract new entrants with the promise of becoming the sole provider for the treatment. The same intellectual property rights prevent new entrants from competing until the patent expires when new entrants can produce generic substitutes. Additionally, a long development time of biotechnology products requires significant private investment. The well-established venture capital market in the U.S. facilitates new entrants. Firms often mitigate new entrants through acquisitions and mergers. Figure 8 summarizes the threat of new entrants in biotechnology.[27]

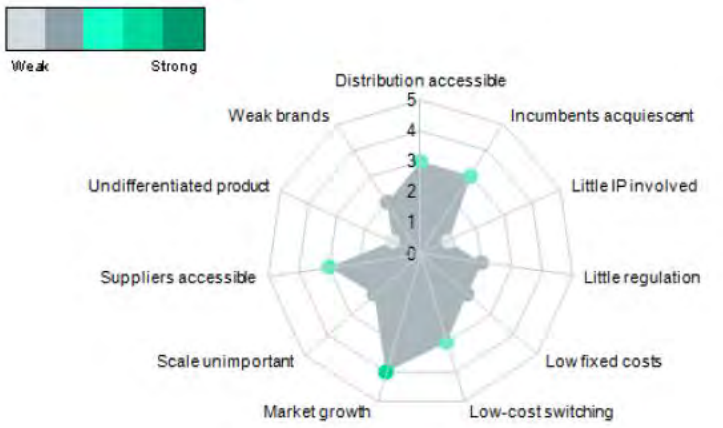


Figure 8: New Entrants

Threat of Substitutes: Buyer propensity for cost-effective therapies makes the threat of substitutes high. Biotechnology products face substitution risk from chemically synthesized drugs (small molecule) and non-pharmacological interventions. The low cost of switching between options enables consumer flexibility, yet there may be risk aversion associated with changing therapies. Intellectual property protection prevents other firms from copying a product

but does not prevent them from developing and offering an alternative product. Figure 9 summarizes the threat of substitutions in biotechnology.[28]

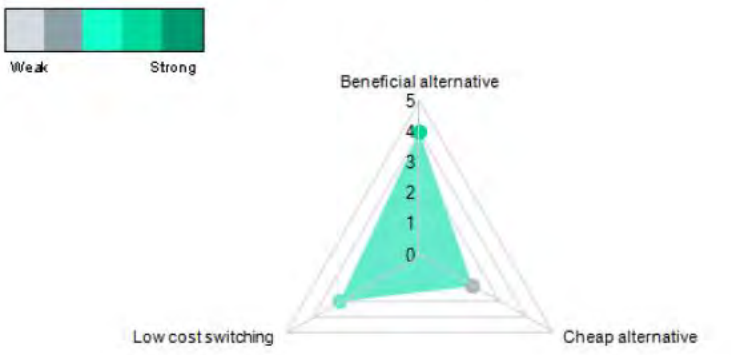


Figure 9: Threat of Substitutes

Rivalry: Developing biotechnology products requires time and resources. The clustered nature of U.S. biotechnology firms creates a competitive advantage allowing firms and academia to operate alongside each other. Thus, competitive rivalry is high in biotechnology as firms jockey to stay aware of competitors' marketing and pricing strategies. These factors promote rivalry and drives innovation. While the market grows, pressure from rivalry decreases. Figure 10 summarizes rivalry in biotechnology.[29]

Figure 10: Rivalry

From this analysis, firms in the human health technologies industry should recognize that buyer power is the driving force when developing firm strategies, with different implications for the size of the firm involved.

Government

The federal government serves two roles in its triple helix relationships with academia and industry. It provides funding as a guaranteed purchaser of human health technologies and as an investor in R&D. It also provides governance through the development of laws, regulations, and policies that support the biotechnology ecosystem. In these roles, the government faces challenges including limited funding, finding the right balance of governance, and overcoming

bureaucracy. The federal government must reconcile these triple helix challenges in order to develop and sustain industry growth.

The government-academia relationship is vital to human health technology ecosystem success. A large part of this relationship is government-funded R&D executed by academia. The government provides these research funds and grants through such programs as the National Institutes for Science, Department of Defense, and Department of Health and Human Services. There are several federal agencies that directly support this academic research, such as the Defense Advanced Research Projects Agency and the Biomedical Advanced Research and Development Authority. Government R&D funds provided to academia result in a knowledge base and human capital expertise used throughout the biotechnology ecosystem. The basic knowledge is used to advance and create innovative human health products while graduating students often become the entrepreneurial workforce needed by industry.[30]

The relationship between the U.S. federal government and the biotechnology industry can be described as symbiotic. However, the relationship also can be antagonistic at times. The relationship requires mandatory cooperation as the human health technologies segment is one of the most regulated industries in the country. Other segments of the biotechnology industry, such as genetic research, agriculture, and energy, are filled with promising emerging and disruptive technologies but lack a similar relationship with the government. Biotechnology emerging technologies have enormous potential for government agencies, such as defense, that will spark further cooperation between the federal government and the industry.

Government regulations play an important role in human health technology. The role is considerable within the industry's pharmaceutical sector, which includes biologics. The U.S. Food & Drug Administration's (FDA) rigorous drug approval process ensures only safe and effective drugs enter the market. The FDA's biotechnology governance makes it one of the most regulated industries globally. Post-pandemic, there will be much attention by both industry and government on how to find efficiencies regarding that governance.

Meanwhile, patents incentivize innovative research and development (R&D) investment by legally protecting intellectual property. Patents and the FDA processes are regulatory pillars of strength for the U.S. providing it competitive economic advantages. Patents are an American Constitutional *ideal* vital to economic growth.[31] Patents spark R&D investment by giving a firm exclusive market rights to inventions for 20 years. FDA processes consume some of the 20 years of patent market rights. While patent law allows a firm to request a patent extension for some of the FDA approval time, exclusive market rights are still likely to be less than 20 years. Therefore, the firm must optimize sales during this exclusive period to recover the R&D costs and create value. This leads to some firms using manipulative patent practices to extend patent time without creating additional value for consumers. The U.S. must balance between strong patent protections to fuel innovation while eliminating non-value-added patent schemes.

A desired outcome in the relationship between academia and government is finding the right balance of effective rules and regulations to drive the right behaviors while not constraining speed and innovation. The ecosystem is vast, but the relationship between academia, industry, and governing agency must be further solidified to ensure future innovation potential is maximized. These relationships are key to the U.S. maintaining the human health technology advantage.

Key Success Factors

The U.S. must retain its innovation leadership in this industry and can do so by prioritizing the ecosystem areas on which to focus. Three areas stand out as essential for success:

G**overnment enablement**, government actions facilitating the biotechnology ecosystem, setting the stage for industry success; **human capital**, manpower required to propel the ecosystem; and **other foundational components**, other aspects of the ecosystem that are essential to the optimization of the industry. All three LOEs serve as stand-alone areas for assessment and improvement, but when combined, offer a more powerful opportunity for the U.S. to continue to lead the world's biotechnology ecosystem.

Government Enablement

U.S. government funding of basic and applied scientific research is falling behind, and China is leaping past the U.S. in public sector science investment. In 1956, U.S. investment in scientific research represented 1.1% of the federal budget and a mere 0.2% of GDP. Sputnik was launched in 1957, and public investment in science surged because of fear of losing the Cold War. Federal science funding peaked in 1965 at 3.6% of the budget and 1.8% of GDP.[32] When comparing gross domestic spending on R&D by all entities (private and public sector) over the past twenty years, the U.S. percent of GDP has increased from 2.63 to 3.07 while China's percent of GDP has increased from 0.89 to 2.24.[33] America's next Sputnik moment is here. China is expected to continue increasing R&D and is quickly closing the biotechnology gaps, while the U.S. continues to support national budget priorities that limit government R&D spending.

The federal government lacks a clear research and development management strategy to maximize product development and help industry successfully bridge the valley of death. A significant stakeholder in federal R&D requirements, the Department of Defense, is developing a roadmap to coordinate research and bridge the valley of death. However, nothing has been produced despite a scheduled release in 2020.[34] By following through on the commitment to develop a roadmap and improve the management strategy, the Department will be more focused on developing biotechnology innovations from basic research. An equivalent plan for the U.S. will also help the federal government make prioritized funding decisions. If the U.S. does not increase and optimize its R&D funding, it risks losing its competitive edge to China, which is outpacing the U.S. in R&D funding. Though R&D is only one piece of the biotechnology ecosystem, it is the key to helping the U.S. maintain its position in the global biotechnology ecosystem.

With the help of Government Enablement and significant industry investment, human health technology is now advancing faster than ethics and regulations. The question is no longer what we can do but what we should do. There is currently no global standard for industry products and their application. The U.S. must lead the world to set ethical standards and norms, make international institutions work.

Small and mid-sized companies would benefit from direct government support through the valley of death and simplifying the engagement process. Regulatory barriers and lengthy approval processes limit success, and unnecessary trade barriers hinder opportunities to bring more human health technologies to market. In addition, more innovation is possible through strategic private-public partnerships. Preventing and monitoring biotechnology threats will require global cooperation through government-led efforts.

Human Capital

The biotechnology ecosystem requires trained researchers, scientists, and lab workers. For sustained human capital to support biotechnology industry growth, the U.S. needs a

sustained pipeline of STEM talent to fill future biotechnology jobs. The U.S. is in a global war on talent. The U.S. must grow its own and attract/retain the best talent from abroad.

The lack of organic STEM education in the U.S. is more about getting U.S. children interested in math and science (the low flow of students into the STEM pipeline) and less about the capacity of the colleges or universities to provide STEM education (the size of the pipe is sufficient). There are already established paths for bachelor, masters, and doctoral degrees at top-notch U.S. colleges and universities, and these institutions "account for nine of the top ten programs in engineering, for eight of the top ten programs for life and medical science, and for seven of the top ten programs for physical science"[35] in the world. Increasingly, community and two-year colleges are playing a role to prepare youth to work in industry involving applications of new and evolving technologies. The COVID-19 vaccine should be used to inspire children into math and science fields like Neal Armstrong's moon landing inspired a generation of children to become astronauts.

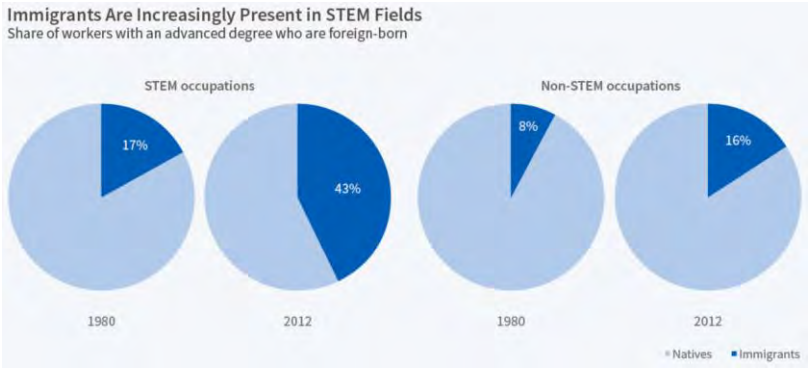


Figure 11: Foreign-Born Workers in STEM Occupations[36]

It will take time to develop an organic STEM workforce, and incentivizing immigrant STEM workers to stay and live in the U.S. with their families will provide the biotechnology industry valuable human capital in the meantime. As shown by Figure 11, immigrants already fill a significant portion of positions in STEM fields. Additionally, in 2017, "foreign students accounted for 54% of master's degrees and 44% of doctoral degrees issued in STEM fields."[37] Barriers exist for non-U.S. citizens to work for the government or a government contractor due to security clearance issues,[38] but this requirement ends while working in the private sector. Even if a biotechnology firm wanted recent Ph.D. graduates, the terms of student visas require students to leave the U.S. within 60 days of the end of their educational program.[39] Every foreign Ph.D. graduate requires an H-1 work visa, which is very limited, making it hard to retain STEM talent. Further complicating matters, STEM workers with Ph.D.s also find employment in postdoctoral positions or other temporary positions, making them unavailable for permanent positions.[40] Additionally, the State Department does not consistently issue work visas to recent graduates. This causes a misalignment of available expertise.

Winning the global war on talent is integral for the U.S. to maintain its advantage in the biotechnology industry. This war is complex, and STEM pipeline changes are necessary to increase the availability of talented, diverse experts to lead and operate this challenging U.S. industry.

Other Foundational Components

The Other Foundational Components are integral pieces of the industry that play an instrumental role in maximizing biotechnology's capacity to solve important global problems and serve as the catalyst to energize innovation in other disciplines and industries. Foundational components are different from government enablement factors. Government enablement can only influence those parameters and control its role in triple helix relationships and government processes that enable clusters, infrastructure, and international trade.

Clusters

Clusters are geographic concentrations of interconnected companies, specialized suppliers, service providers, and associated institutions in a particular field that are present in a nation or region. Clusters arise because they increase the productivity with which companies can compete. Therefore, the development and upgrading of clusters is an important agenda for governments, companies, and other institutions."[41] For the U.S. human health technologies industry, clustering creates a competitive advantage.

The U.S. is home to the most powerful biotechnology clusters in Boston, Philadelphia, Los Angeles, and Silicon Valley. With the recent COVID-19 pandemic, these clusters benefit economically from increased private and federal funding for human health technologies, leading to significant employment opportunities that will spur future advances and innovations for human health and defense. For example, a recent McKinsey & Company article showed that funding exploded in biotechnology since January 2020. Venture Capital activity grew by 45% or to $36.6B in 2020, deals such as partnerships, joint ventures, or licensing agreements grew 84% or $170B. Finally, IPOs grew the fastest, with companies raising 187% over 2019, or $34.3B.[42] These investments will also help improve infrastructure in these cluster areas to drive more innovations.

Infrastructure

Human health technology firms rely on critical infrastructure to operate, and internet-based services are especially vital. However, the U.S. lacks consistent deployment of broadband internet services. The FCC defines *broadband internet service* as speeds at least 25 megabits per second for downloads and three megabits per second for uploads.[43] Biotechnology firms generate a lot of data. For example, the size of an electronically stored human genome reaches 200 gigabytes. At 25 megabits per second, the human genome would take 18 hours to download. But most importantly, in order to upload the human genome, at three megabits per second, the human genome would take over six days to upload.

Commercial internet providers do offer higher speeds. Xfinity provides download speeds of 1000 megabits per second and upload speeds of 35 megabits per second.[44] With these speeds, upload time for the human genome reduces to only 13 hours. Because the volume of data for experiments can exceed a terabyte, upload time approaches three days, making overnight shipping a physical hard drive faster. Verizon FIOS offers upload speeds of 880 megabits per second.[45] At this speed, upload time for a terabyte reduces to 2.6 hours. However, Verizon offers FIOS only in portions of New Jersey, New York, Maryland, Delaware, Massachusetts, Rhode Island, Virginia, and Washington DC.[46] To facilitate transportation of biotechnology data, the U.S. Government should invest in increased broadband capacity.

International Trade

International trade is essential for driving higher profitability and optimizing supply chains for the human health technologies ecosystem. Increasing international trade is important to the U.S.'s success in the human health technologies industry.

International trade increases business activity in the human health technologies sector, and higher profits increase economic growth. Exports and imports in the human health technology industry will significantly increase in the coming years as the U.S. and other countries establish adequate regulatory environments. Additionally, during this time, the number of companies mature enough to manage and regulate imports and exports will also increase. Demand facilitates this growth in wealthier countries where citizens can purchase products not covered by national health systems.

Successful international trade is also dependent on resilient and robust supply chains. International regulatory barriers do limit some trade opportunities. For example, Europe limits most genetically modified organisms (GMOs) that are used throughout the U.S. However, international trade opportunities are increasing through increased supply chain development. For example, U.S. companies collaborate with supply chain partners outside the U.S. as they seek specialized skillsets or cheaper production costs. Unfortunately, international supply chain relationships are open to risk. As seen with the COVID-19 pandemic response, many supply chain bottlenecks occurred to include personal protective equipment (PPE), testing swaps, vaccine ingredients, and vaccine vials. Balancing production costs that impact profits and access to materials continues to be important.

A significant risk in the supply chain, especially in industries like human health technology that transfer information through multiple companies during the research and development of a product, is intellectual property (IP) theft. As an IP-intensive industry, protecting human health technology IP is difficult but crucial to protecting profits and technology that could potentially be tied to U.S. national security. Limited IP protection exists from international organizations like the World Trade Organization (WTO) but is enhanced by country-level international trade agreements.

The human health technology industry will continue to engage in significant international trade due to profitability and supply chain requirements. Therefore, companies continue to rely heavily on IP protection. Without adequate protection at all levels to include WTO, human health technology companies risk losing significant profits through theft of proprietary information.

Great Power Competition & Porter's Diamond

Biotechnology is a new frontier in the technological competition between the United States, Russia, and China. Russia's marketing of its Sputnik V through bilateral agreements with other countries is the latest means the Russian Federation uses to secure diplomatic influence while simultaneously gaining a foothold in the global pharmaceutical market. Though still behind the United States in real terms, China's biotechnology industry is transforming domestic sectors from medicine to military, thanks to the country's symbiotic civil-military relationship, which imposes fewer constraints on the application of disruptive technologies.

Russia

Russia's "vaccine diplomacy" and the challenges of the World Health Organization's COVAX Facility to meet the demand globally for approved COVID vaccines have the potential to increase the attractiveness of more autocratic forms of government such as Russia's and dampen America's 'preferred partner' status. Additionally, Russia could leverage its regional pharmaceutical clusters and tech companies to produce mass-casualty bioweapons on a large scale. Russia uses strategic partnerships between domestic and multinational pharmaceutical companies in the country to address an infusion of human capital and investment in R&D. However, Russia currently shows only limited regional biotechnology industry success resulting in limited global influence.

The study of Russia's biotechnology Porter's Diamond factor shows the ecosystem is expanding but currently operating under immature conditions. Russia's complex regulatory landscape emphasizes the localization of the production of medicines and favors domestic pharma companies. Russia has a brain drain due to the declining number of Russian students with advanced degrees and immigration. Russia does employ regional pharmaceutical clusters, with the most successful ones located in Moscow, Kaluga, and St. Petersburg-Leningrad region. Additionally, Russians' high smoking rate, alcoholism, increased life expectancy, and the aging population drive demand for new medicines and market growth. Russia's health care system is inefficient and costly, but it has tried to strengthen its manufacturing practices to boost global exports—targeting Central East European countries initially. Russia is also stimulating the local market by limiting foreign company access.

Russia's use of chemical weapons continues to silo Russia outside the community of nations as a trusted partner. Russia's deft manipulation of the worlds of biotechnology—including pharmaceuticals—and the geopolitical environment will continue to challenge the internationally recognized U.S.-led "rules-based" world order.

China

The study of the Porter's Diamond factors as they apply to China's biotechnology industry reveals that its ecosystem is dynamic but immature. The ecosystem is supported by two key pillars: top-down government approach and interaction with multinational and foreign companies. The role of the government as an influencing determinant is prevalent. Despite existing huge biotechnology clusters, the firm strategy, structure, and rivalry factor is not favorable since the regulatory environment impair collaboration and interaction among domestic and foreign firms. The demand conditions factor, in turn, is domestically favorable due to the large and increasing market; but, in terms of exports, the low quality of products and the counterfeits harm the Chinese possibilities of increasing its share in the global biopharmaceutical market.

China has structured biotechnology clusters in the related and supporting industries, where the triple helix (government-academia-industry) model may evolve. Nonetheless, the factor is not favorable. The existing skepticism regarding the regulatory environment and the government's interference still undermine the biotechnology industry of China. Finally, conditions factors are, as the others, not favorable. The main issue is human capital since China depends on contracting overseas researchers or training its workforce in international universities.

Therefore, notwithstanding recent progress in biotechnology, based on the Porter's Diamond analysis, China still has a long way to go to compete with the U.S. or even meet its own domestic demand.

Biotechnology and Ethics

With its focus on human health technologies and pushing the boundaries of science to increase human health and life spans, biotechnology can elicit fear and concern that humans are gaining too much power and trigger debate for more oversight and ethical frameworks. The science behind genomic editing and CRISPR is accelerating opportunities for dual-use applications of these emerging technologies, prompting questions along the way about incentives, intentions, and actions. Appendix B provides a discussion on ethical views and relationship to biotechnological applications.

STRENGTHS, WEAKNESSES, OPPORTUNITIES, AND THREATS ANALYSIS

Human health technologies benefit from several strengths. While many sectors suffered during the economic downturn caused by the COVID-19 pandemic, the human health technologies sector continued to thrive. This attracted investment capital to hedge against risk in other industries. The biotechnology industry proved its ability to thrive in even the most limiting environments.

Weaknesses in the biotechnology industry hinder growth. Human capital and government enablement (or lack of enablement) markedly impact the industry. The biotechnology industry requires significant investment in labor. Research laboratories and production lines require skilled STEM workers. However, U.S. institutions of higher education awarded nearly half of all graduate-level or higher degrees to foreign nationals.[47] In sum, this limits the supply of workers for the industry. The U.S. infrastructure also hinders growth. The FCC broadband 2015 standard of 25 megabits/second download and 3 megabits/second upload speeds require updating. Slow broadband speeds and limited 5G rollout result in data transmission rates slower than physically shipping hard drives. Last, as supply chains become more specialized, any disruption to logistics impacts the industry.

Opportunities for the biotechnology industry would benefit from government enablement. As populations age and access to healthcare increases within healthcare, the biotechnology industry will see increased revenue growth.[48] To enable the earth's limited resources to support a growing population, more efficient agriculture and aquaculture, and medicines for disease detection, prevention, and treatment will require innovation, often from biotechnology. To maximize success in these areas, the biotechnology industry requires more efficient regulatory processes, sound government strategy, and consistent, sufficient funding. This requires coordinated and directed efforts by the government and presents opportunities for increased revenue that will fuel innovation in the industry. Further, optimization of STEM education and immigration will provide the right workers to the right companies.

Major threats include the high cost and time required to develop human health products threaten success. Timely regulatory approval remains a burden. The Chinese Communist Party set biotechnology as one of its strategic pillars. As the biotechnology industry grows within China, competition for skilled workers will increase pressure on the labor supply. Additionally, as the industry grows, demand will increase on limited supplies of APIs and inputs to the production process.

COVID-19 – A CASE STUDY IN SURGE AND MOBILIZATION

Responding to the next pandemic will require a strong human health technology base that can surge and mobilize faster than it did with COVID-19. COVID-19 was considered a simple virus, and the next pathogen could be much more dangerous. Global cooperation and a global health technologies ecosystem will be necessary to stop it at its origin to prevent devasting life and economic impacts.

The COVID-19 global pandemic is a momentous opportunity for the human health technology industry. The U.S. federal government successfully mobilized and partnered with the biotechnology industry to speed up the development of a vaccine and work towards improving therapeutics and medical testing resources. The federal government created a White House Task Force, Operation Warp Speed (OWS), to help the sector lower barriers such as funding to expedite the research and development of vaccines and troubleshoot the logistics of delivering the vaccine as quickly as possible. Other vulnerabilities the pandemic exposed include issues with the organic supply chain and the ability to surge production of medical and testing equipment. There are few bright spots with a global pandemic except for the widespread realization of biotechnology's importance and the need to further develop government and the biotechnology industry's relationship. The industry is growing at a pace that if the federal government waits, the lack of public trust may stall further advancements that are advantageous to all human beings and U.S national security.

COVID-19 saw many issues with biotechnology supply chains. These issues included limited access to critical active pharmaceutical ingredients (API), material shortages like personal protective equipment, ventilators, vials for vaccines, or logistical and transportation issues to speed up access to manufacturing or distribution of medical products. The OWS Task Force was established as a whole-of-government response mechanism to help minimize and overcome these complex supply chain and manufacturing capacity issues.

Another area highlighted by COVID-19 that will outlast the pandemic is the shift in trade behaviors. In February 2021, President Biden signed *Executive Order on America's Supply Chains* to "help create more resilient and secure supply chains for critical and essential goods." This Executive Order states: "while we cannot predict what crisis will hit us, we should have the capacity to respond quickly in the face of challenges. The U.S. must ensure that production shortages, trade disruptions, natural disasters, and potential actions by foreign competitors and adversaries never leave the U.S. vulnerable again."[49] Adequate supply chain and trade processes and policies are essential to U.S. national security. The U.S. must find the balance between free-market forces and the cost required to secure a dedicated supply chain and trade environment.

Finally, COVID-19 shows the importance of the right policies to drive the proper functioning of the human health technologies ecosystem to drive innovations. Focused, strategic, government enablement was essential. For example, OWS was the key to the successful U.S. vaccination program. The program shows the importance of having the right people with the right skillsets across the triple helix. It shows the importance of winning the global war on talent. For example, the mRNA technology platform used for the Pfizer vaccine was developed by Turkish immigrants accepted into Germany who launched the company BioNTech. On the negative side, government policies led to supply chain disruptions that slowed innovation and the overall response to the pandemic. Additionally, nations took stovepipe approaches to address a global pandemic that is still not under control, and new variants threaten the global community daily.

POLICY RECOMMENDATIONS

The Eisenhower School Biotechnology Industry Study examines biotechnology's human health technologies sector to understand the impacts, implications, and effects on U.S. national security. By examining the strategic forces that apply to this section of the biotechnology industry and applying the three lines of effort, the Industry Study created and evaluated proposals to improve the U.S. government's support of this sector of the economy. The recommendations are listed below:[50]

1. (Government enablement) The U.S. should establish the Office of Science and Technology Policy as a permanent cabinet-level position and define its roles and authority. The USG currently lacks a central coordination authority to direct and promote the Science & Technology ecosystem, including human health technology. This recommendation is considered budget neutral as existing resources can be re-allocated. Political resistance has prevented this in the past, but COVD-19 highlights the importance of this function for economic and national security.
2. (Human Capital) The U.S. should simplify grant processes, so academia stimulates STEM youth engagement to fill STEM pipelines. Biotechnology requires a continuous flow of qualified and trained workers. The flow or entry of interested youth must be increased to ensure a sufficient qualified labor force. This recommendation requires minimal time and costs as this is a procedural revamp to ensure ease of grant application and immediate provision of funds to engage youth and encourage STEM pipeline fill. The weakness of this recommendation is that it is dependent on state governments for execution.
3. (Human Capital) The U.S. should change student visas to allow accompanied temporary residency during STEM education and issue a work visa or permanent resident card upon graduation. The STEM pipeline includes international students that must depart within 60 days of graduation. This depletes the U.S. knowledge base and fosters foreign innovation. Retention of educated international students ensures diversity and increased knowledge within domestic firms. Resources required to execute are marginal to support the existing rewrite of immigration policy and regulation. The weakness of this recommendation is that immigration is a contentious topic, and there is a danger of this being lumped in with comprehensive immigration reform. While understandable, the length of time for that reform will not support the biotechnology requirements.
4. (Government enablement) The U.S. should increase federal funding of research to at least 1% of the gross domestic product to preserve the U.S. lead in human health technologies prioritizing basic research. Basic research conducted in academia is a crucial enabler of the biotechnology ecosystem enabling innovation and product development. This recommendation is expected to cost $64B per year and will increase government expenditures. The weakness is that this will increase the National Debt unless it is determined that reductions in the DoD budget should be considered, which will face great political resistance.
5. (Government enablement) The U.S. should lead a global cooperative effort to update international trade agreements and World Trade Organization standards and intellectual property rights and data policies. Existing agreements and global standards do not align with current industry practices. The resourcing requirements for this recommendation are marginal, requiring only updates to language, policy, and regulations. The weakness of this recommendation is the limited bandwidth of organizations, which may delay

development. Additionally, there is no common understanding of the problem or solutions that can form the basis of an agreement. The international community simply cannot agree.

6. (Other Functional Components) The U.S. should incentivize the synthetic biological production of critical APIs through short-term qualifying research expenditure tax credits to diversify risk and reduce foreign dependency. Active pharmaceutical ingredients are required for manufacturing medicines, but domestic production of critical APIs is insufficient to meet the required demand. This recommendation will be resourced with short-term corporate tax credits based on qualifying research expenditures. These credits are carriable for up to 20 years but are limited in scope and application. The weakness is that biological processes may not be known or feasible for desired APIs. Additionally, tax credits may not be enough to incentivize companies to develop synthetic APIs.
7. (Other Functional Components) The U.S. should incentivize private firms to establish broadband internet capabilities of at least 800-megabit download / 800-megabit upload capability. Data requirements for biotechnology are large and exceed the capabilities of most broadband services. This recommendation will utilize money within the Infrastructure Bill (approximately $100B) to provide new market tax credits for broadband providers meeting the minimum requirements stated. However, this Bill may have insufficient funds to cover the required work.

CONCLUSION: A WAY FORWARD

Biotechnology's ability to help solve the most vexing challenges enabled the U.S. to marshal industry, academia, and government to respond to a global health crisis and ensure the country is better prepared for future pandemics. As an engine of economic growth, biotechnology has created billions of dollars of real-market opportunities for the U.S. economy. This trend is expected to continue in the decade and beyond.

The potential of the future U.S. biotechnology industry is enormous. Innovations in the biotechnology industry, such as synthetic biology and genomic medicine, are producing cross-over commercial and defense applications that will continue to shape and redefine the future of the industry. The U.S. Government is best positioned to engage biotechnology stakeholders to manage threats in the misuse of these technologies and ensure translational research contributes to useful solutions that benefit all Americans.

The U.S. biotechnology ecosystem is strong. However, sustaining biotechnology innovation will necessitate a U.S. government strategy to address attendant challenges such as ensuring a responsive regulatory environment, rooting a pipeline for a skilled workforce, securing sustainable investment streams to bridge the valley of death, and creating incentives for industry to partner with government more efficiently. Further, as great power competitors such as China leverage its biotechnology sector to challenge an open international system, the U.S. will need to strengthen relationships with allies and partners to reaffirm effective international norms that support a globalized biotechnology industry. Last, the impact of COVID-19 showed that next-generation supply chains would need to factor in elements such as APIs that are part and parcel of biotechnology.

With its proven ability to improve so many aspects of health, biotechnology shows tremendous potential to play an even larger role in a vigorous U.S. economy. Going forward, the USG can target public investments to shape the biotechnology ecosystem for continued success as an economic driver and a force for good. The fact-based analytical recommendations in this paper will bring broad benefits to U.S national security and the warfighter.

APPENDIX A: RECOMMENDATIONS AND PRIORITIZATION

Recommendation 1	Establish the Office of Science and Technology Policy as a permanent cabinet-level position and define its roles and authority.
Key Success Factor	Government Enablement
Problem Statement	USG currently lacks a central coordination authority to direct and promote the Science & Technology ecosystem, which includes human health technology.
Risk	An uncoordinated approach by the U.S. government results in suboptimized results and support.
Gaps	Although biotechnology has been identified as a national priority within the Interim National Security Strategy and several other policy documents, there is no lead designated with the power to direct and enforce alignment.
Owner	President
Coordination	OSTP, Congress
Resources	Budget neutral
Weaknesses	Political resistance

Recommendation 2	The U.S. should simplify grant processes so academia stimulates STEM youth engagement to fill STEM pipelines.
Key Success Factor	Human Capital
Problem Statement	Maintaining a filled pipeline of STEM students and workers
Risk	Required component for biotechnology, with limited workers availability there is associated production and innovation limits.
Gaps	The available pipeline is greater than the interested youth.
Owner	Department of Education
Coordination	National Science Foundation
Resourcing	Minimal time and costs required, this is a procedural revamp to ensure ease of grant application and immediate provision of funds to engage youth and encourage STEM pipeline fill.
Weaknesses	Dependent on successful revamp, assumes with greater engagement the pipeline is filled, and ignores industrial potential.

Recommendation 3	Change student visa to 1) allow accompanied temporary residency during STEM education, and 2) upon graduation, a work visa and/or permanent resident card is immediately granted.
Key Success Factor	Human Capital
Problem Statement	Retaining foreign educated students in the U.S. labor force ensuring the knowledge bases stays within the U.S.
Risk	Academia provides the basic research and knowledge of biotechnology. When students are not retained within the U.S., the knowledge departs with them. Innovation from that

	knowledge then is generated in foreign economies and decreases the capabilities of our clusters.
Gaps	Current immigration policy does not allow retention of students and associated knowledge.
Owner	Department of Homeland Security
Coordination	Congress, DOS, HHS, DOJ, DOEd, DOL, and Industry, National Institutes of Science
Resources	Marginal to support the existing rewrite of immigration policy and regulation.
Weaknesses	Immigration is a contentious topic and there is a danger of this being lumped in with comprehensive immigration reform. While understandable, the length of time for that reform will not support the biotechnology requirements.

Recommendation 4	Increasing Federal research funding to at least 1% GDP, with associated prioritization of biotechnology, preserves the U.S. lead in innovation.
Key Success Factor	Government Enablement
Problem Statement	Basic research resides in academia and generates the required innovation for the biotechnology ecosystem.
Risk	Basic research and disruptive innovation is required for biotechnology. Corporate research is not driven within shareholder economics and is sub-optimized. Additionally, shareholder economics promotes retention of knowledge vs sharing.
Gaps	Federal share of research and development funds are continuing to decline representing 0.6% of GDP, of which 0.1% is directed towards basic research.
Owner	Congress
Coordination	Presidential Budget Request
Resources	The funding increase of 1% GDP reflects an approximate increase of $64B. The U.S. should increase federal funding of research to at least 1% of the gross domestic product to preserve the U.S. lead in human health technologies prioritizing basic research. This recommendation is expected to cost $64B per year and will increase government expenditures.
Weaknesses	This will increase the National Debt unless it is determined reductions in DoD budget should be considered which will face great political resistance.

Recommendation 5	Lead global cooperative effort to update international trade agreements and World Trade Organization regarding data and intellectual property rights. F
Key Success Factor	Government Enable

Problem Statement	Existing agreements and global standards do not align with current industrial practices.
Risk	Intellectual property protection, services, and data flows are conducted and are at risk from misaligned trade policies and agreements.
Gaps	The WTO does not have policies (or effective ones) to deal with data and IP protection.
Owner	Department of Commerce, Trade Representative
Coordination	Department of State, WTO, etc.
Resources	Marginal, this is an update to language, policy, and regulations.
Weaknesses	Limited bandwidth of organizations may delay development. Additionally, there is no common understanding of the problem or solutions that can form the basis of an agreement. The international community simply cannot agree.

Recommendation 6	Increase SynBio production of critical active pharmaceutical ingredients and materials to diversify risk and reduce foreign dependency.
Key Success Factor	Other Functional Components
Problem Statement	APIs are required for pharmaceutical manufacturing.
Risk	Critical APIs supply may be removed by government actions.
Gaps	Domestic industrial base cannot supply sufficient critical API production capabilities.
Owner	Industry
Coordination	Department of Commerce, National Institutes of Science, Department of Health and Human Services (FDA)
Resources	Short term corporate tax credit based on qualifying research expenditures. These credits are carriable for up to 20 years but are limited in scope and application.
Weaknesses	Biological processes may not be known or feasible for APIs. Additionally, tax credits may not be enough to incentivize companies to develop synthetic APIs.

Recommendation 7	Incentivize private firms to establish a broad-band internet of at least 800 mbit download / 800 mbit upload capability.
Key Success Factor	Other Functional Components
Problem Statement	Data requirements for biotechnology are large and exceed the capabilities of most broadband services.
Risk	Data transfer conducted by sneaker-net is limited to international travel (conditions and government permission)
Gaps	1) STEM outreach and programs require broadband 2) Biotechnology ecosystem requires sufficient broad-band capability
Owner	Federal Communications Commision

Coordination	Department of Commerce, Department of Homeland Security
Resources	Utilize money within the Infrastructure Bill (approximately $100B) to provide new market tax credits for broadband providers meeting the minimum requirements stated.
Weaknesses	Insufficient funds for required coverage.

Comparative Weighting	Comparative Score			
Recommendation	Cost	Immediacy	Expected Result	Total
Promote the biotechnology ecosystem as part of the national research and triple helix innovation strategy by defining the roles and authority of the Office of Science and Technology Policy as a cabinet-level position.	5	5	6	16
Ensure universities, two-year colleges, and educational programs have simplified grant processes to create STEM youth engagement pipelines.	6	6	3	15
Change student visas to both allow accompanied temporary residency during STEM education and issue a work visa or permanent resident card upon graduation.	4	3	4	11
Increase federal funding of research to at least 1% of gross domestic product, with associated prioritization of biotechnology, to preserve the U.S.' lead in knowledge and innovation.	0	4	5	9
Lead global cooperative effort to update international trade agreements and World Trade Organization standards and policies regarding intellectual property rights and data.	3	1	2	6
Incentivize the synthetic biological production of critical API to diversify risk and reduce foreign dependency.	2	2	1	5
Incentivize private firms to establish a broad-band internet of at least 800-megabit download/upload for all users including subject matter experts.	1	0	0	1
	Higher Score is Better			

APPENDIX B: RESEARCH METHODOLOGY

This paper is a result of information learned during they AY 20-21 Biotechnology Industry Study. This study consisted of 20 virtual classroom lessons, 32 guest lectures in either individual or panel formats, one interactive exercise, domestic field studies of two biotechnology sub-industries, and two virtual international engagements. From January through April, the IS engaged in a series of lessons to review the concepts of business strategies and analysis, international economics, and industrial base policy and implications. The content was further extended through a series of guest lecturers and discussion. Two exercises were critical in understanding the research and development process, while domestic field studies and virtual international travel allowed the seminar to examine specific industry concepts, policies, and international implications of Great Power Competition. Each student wrote individual papers to further analyze specific topics of the biotechnology industry that became a great foundation for this group paper. The following individual papers were utilized extensively to develop this paper.

Commander Michael Barna	"National Security Implications of Naturally-Occurring and Synthetically-Engineered Biothreats"
Mr. Peter Battaglia	"Applying Porter's Diamond: Promoting the Department of Defense Biotechnology Industrial Support"
Ms. Stephanie Cabell	"Russia's Emerging Pharmaceutical Sector in an Era of Great Power Competition"
Colonel Gelson de Souza	"Brazilian-Chinese Triple Helix Comparison"
Commander Thomas Eisenstatt	"The Status of the Biotechnology Industry"
Colonel Maureen Farrell	"Human Perfomance and Biotechnology"
Mr. Timothy Hale	"Developing Relationships Between the Government, the Biotechnology Industry in Fostering Public Trust"
Ms. Georgene M. Kalogeras	"Ethical Considerations in the U.S. Biotechnology Industry: National Security, Privacy, and Consumer Protections in Directo-to-Consumer Genetic Testing"
Mr. Sampel Khouvilay	"Promoting Biotechnology"
Lieutenant Colonel Sarah Lenz	"Ethics and the Future of Warfare"
Lieutenant Colonel Nadine Nally	United States Army
Colonel Karl Painter	"Iron (U.S) sharpens Iron (Europe) – Maintaining Global Leadership in Biotechnology"
Ms. Jadee Purdy	"The Biotech Industry Performs Well Under Pressure: A Surge and Mobilization Analysis"
Lieutenant Colonel Jason Schenck	"Steps to Approval: FDA Regulation & Patents"
Colonel Natasha Stanley	"Industry Study International Review Singapore"
Lieutenant Colonel Norbert Toth	"Pharmaceutical Industry in the European Union"

APPENDIX C: BIOTECHNOLOGY AND ETHICS

Biotechnology, with its focus on molecular biology and pushing the boundaries of science to increase human health and life spans, can elicit fear and concern that humans are gaining too much power, and trigger debate for more oversight and ethical frameworks. The science behind genomic editing and CRISPR is accelerating opportunities for dual-use applications of these emerging technologies, prompting questions along the way about incentives, intentions, and actions. The ethical principles of utilitarian (produce greatest good and least harm) and social benefit (in what way will society benefit) need to guide both research and legitimate application of biotechnology's benefits.

National security is continually evolving to adapt to threats as they appear. What national security looked like before 9-11 is different than how it is perceived in 2021. This type of evolution is expected and can be seen most recently in how the U.S. has reacted to the COVID-19 pandemic. One topic brought to the forefront because of the pandemic is the threat of bioweapons and bioterrorism. Ethical concerns regarding bioweapons must be thoroughly dissected and understood to plan for what may lie ahead.

Dual-use research is a concern when examining the ethics of bioweapons. Legitimate scientific research can be utilized for remarkable developments in medicine. However, the "deliberate misuse of knowledge generated by legitimate scientific research" can be used for biological weapons proliferation which can be a threat to public health and national security. This opens the door to new and harder-to-detect bioweapons being created, sometimes unintentionally, leading to malicious use.

There is an inherent risk of human error within laboratories. When limited oversight is present and a lack of adequate understanding of the probability of dual-use technologies are present the risk increases. Some of the human errors that can result in bioweapon release are laboratory accidents that result in pathogen release, laboratory-acquired infections that may be communicable to the community, and unexpected results of experiments.

One of the scientific community hallmarks is a commitment to information share to both accumulate and disseminate scientific discoveries in a collaborative effort. Research shared can serve as a building block to other research, furthering scientific discovery and benefits to the overall public.[51] Publishing, while seen as a usual step in the scientific process, could be utilized by rogue actors to create a bioweapon or the like; lack of publishing could prevent further discovery of beneficial treatments and protocols. This is an ethical dilemma biologists must contend with when publishing.

Policy regarding bioweapons and their ethical use are generalized. This can be because the U.S. government lacks clear definitions across all governmental agencies for biodefense, biosecurity, and biosafety. Articulated definitions are the first step to a policy that will serve the purpose it intends.[52] Additionally, the U. S. must establish a national database on unintentional releases of pathogens from labs, both private and governmental.[53] While the primary agents of bioweapons, like anthrax, have been studied extensively, there must be studies on all pathogens.

Education for researchers on accepting ethical responsibility to avoid bioweapon advancement is vital for facilitating personal responsibility in a lab setting. Understanding unintended social consequences of research will change the research culture moving forward. Identifying a method for all researchers to reveal to authority's potential bioterrorist threats in their labs is also crucial in advancing ethical behavior in labs and securing a solid research culture moving forward.[54]

To keep the adversaries of the U.S. from taking advantage of the COVID-19 pandemic or other pathogens and formulating a bioterrorist attack in the future, there must be a whole of

government approach to standardize ethics to help most effectively counter this national security threat.

APPENDIX D: FIRM BRIEFS

AstraZeneca

Stephanie Cabell
Georgene Kalogeras
Natasha Stanley
Norbert Toth

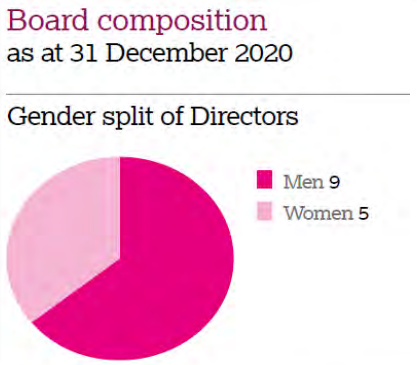
Agenda

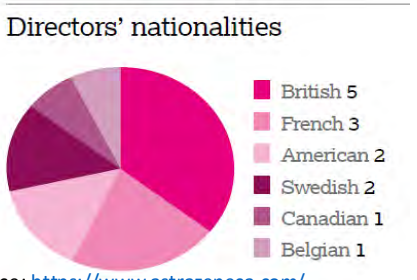
- **AstraZeneca Basic Information**
  - Company Profile
  - Company History
- **AstraZeneca Inside Activity**
  - Business and Market Strategy
  - Research and Development and Innovation Initiatives
  - Strategic Game Board
  - Ethics, Human Capital, and Industry Change
- **AstraZeneca Business and Financial Execution**
  - Financial Analysis, Value/Risk Analysis, and Peer Competitors
  - Porter's Five Forces
  - Supply Chain Assessment
- **U.S. Policy Options and Recommendations**

Company Profile

- **Business Description:** biopharmaceutical company that develops, manufactures and markets prescription pharmaceuticals and biological products in three therapeutic areas.

- **Company HQ:** CAMBRIDGE, United Kingdom
- **Incorporation/Establishment:** 1999.
- **Workforce:** 76,100 (**13,400 in US**)
- **Key Employees:** Chief Executive Officer/Director: Pascal Soriot, Chief Financial Officer/Director: Marc Dunoyer, Chairman: Leif Johansson (Σ: **14 directors**)
- **Global presence:** 26 operations sites in 16 countries.





Source: https://www.astrazeneca.com/

Strategic priorities:

1. Delivering growth and therapy area leadership.
2. Accelerating innovative science.
3. Being a great place to work.

Company History

- **"Marriage of Equals":** 1999 Astra AB + Zeneca PLC = AstraZeneca PLC.

- **2000-2006:** small scale M&A and collaboration
- **2007-2012:** challenges and opportunities:
  - patent expiry;
  - more collaboration & acquisition (e.g., Arrow Therapeutics , MedImmune, Novexel Corp).
- **2013-…:**
  - restructuring;
  - cutting down on jobs, focus on fewer therapeutic areas;
  - rejecting Pfizer;
  - new R&D strategy;
  - continue own M&A agenda (acquisition of Alexion Pharmaceuticals in the third quarter of 2021.)

The AstraZeneca Corporate HQ (Cambridge, UK)

source
locatio

Source:
https://blogs.mercurynews.com/collegesports/2016/07/21/big-12-pursues-expansion-preview-next-big-realignment-wave/

Business and Market Strategy

- **Highly competitive market with** a lot of competitors and **high entry barriers** that requires:
  - significant capital, extensive investment in R&D and innovation, infrastructure, highly skilled and educated labor force, access to clinical trials...

- **AstraZeneca's comprehensive strategy includes:**
  - strong product portfolio;
  - focus on R&D and M&A projects and collaboration;
  - leveraging:
    - global presence;
    - triple helix model of innovation.

Some of the significant Competitors:

In Europe: F. Hoffmann-La Roche Ltd, Novartis AG (Switzerland); Sanofi (France)

In US: Pfizer Inc., Amgen Inc., Gilead Sciences Inc., Merck & Co Inc, AbbVie Inc

Therapeutic areas:

1. **Oncology**
2. Respiratory & Immunology
3. Cardiovascular, Renal and Metabolism (CVRM)

\+ Other Medicines and COVID-19

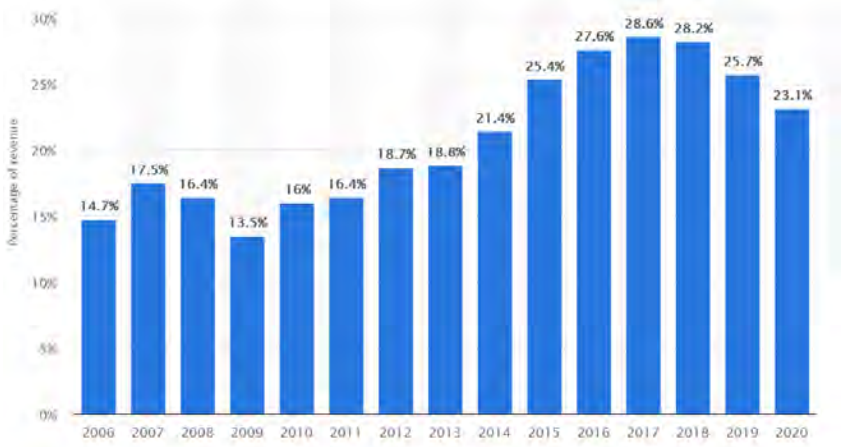
Source: https://myventurepad.com/why-you-should-create-an-rd-team-in-your-company/

AstraZeneca locations

source: https://blog.zymewire.com/post/from-a-to-z-a-map-for-selling-to-astrazeneca

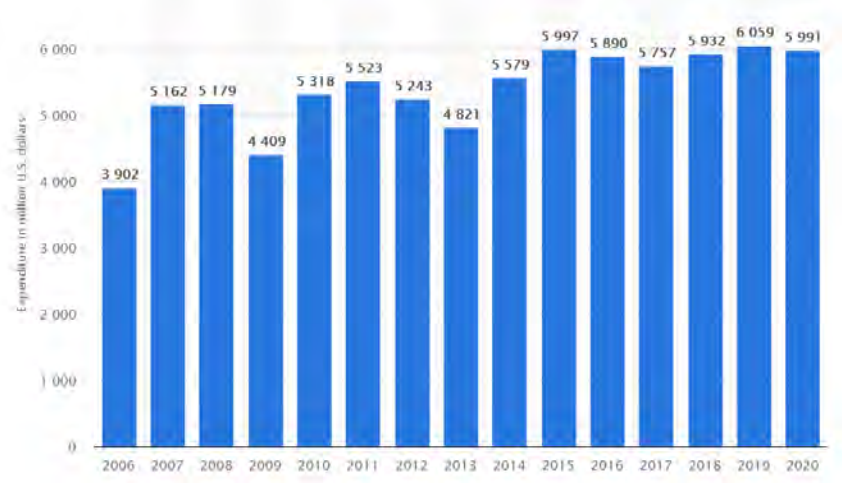
Research and Development (R&D)

- In 2010, AZN created a new 5R (right target, right patient, right tissue, right safety, right commercial potential) Framework.
- AZN established two therapy-focused R&D organizations:
  - Oncology R&D;
  - BioPharmaceuticals R&D.
- AZN focuses on collaboration in R&D.
- AZN has 9 strategic R&D centers (4 in U.S., 2 in UK, 1-1 in China, Japan and Sweden).
  - 3 biggest R&D centers: Cambridge (UK), Gaithersburg (USA); Gothenburg (Sweden).
- R&D organizations employ 10,500 workforces.
- In 2020, 23% of AstraZeneca's total revenue was expended on R&D (amongst the top five companies).



R&D expenditure as a percentage of total revenue

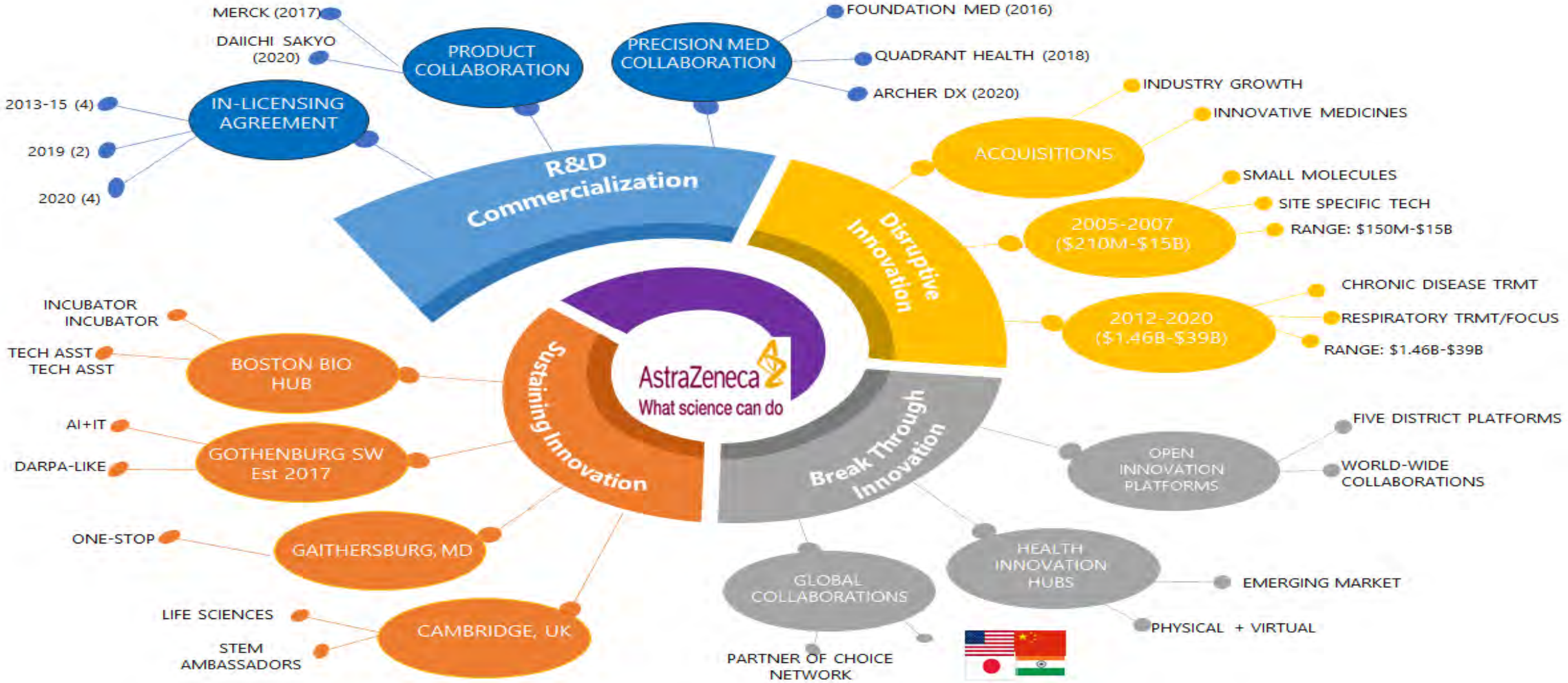
source: https://www.statista.com/statistics/266561/rundd-expenditure-of-astrazeneca-as-percentage-of-revenue-since-2006/



Expenditure on R&D from 2006 to 2020

source: https://www.statista.com/statistics/266556/expenditure-on-research-and-development-of-astrazeneca-since-2006/

Innovation Eco-System



Strategic Game Board

Where to compete:

- wide product portfolio & diverse markets:
  - decreases the company's exposure to certain risks.

+ geographic diversity provides proximity to customers.

How to compete:

- focusing on R&D and collaboration;
- leveraging the benefits of the triple helix model of innovation;
- exploiting the global footprint and strong therapeutic portfolio;
- offering green solutions (thinking long-term).

When to compete:

- constant competition as a result of R&D, collaboration, and M&A (e.g., in 2020 AZN secured **29** approvals for new medicines,).

Ethics, Human Capital, and Industry Change

- **Ethics: Rebuilding Trust in the Pharmaceutical Industry**
  - Recognition and concern about healthcare disparities by race, region, and socioeconomic status as well as impact of climate change on public health
  - Addressing through embedding a culture of ethics and integrity, adopting higher governance standards, partnering across sectors, setting ambitious sustainability targets, and improving relationships with employees, shareholders, and other stakeholders.

- **Human Capital**
  - Strides in diverse recruitment
  - Culture of lifelong learning and development
  - Women comprise of 50.5% of global workforce and 46.9% of senior roles
  - Removed performance ratings to focus on coaching, development and contribution
  - Ethnicly diverse leadership
  - Investment in online learning and education

- **Industry Change**
  - Sustainability
    - Sourced 99.9% of imported electricity globally from renewable sources
    - Post-pandemic influence on workplace flexibility options
  - Fetal/animal testing changes
  - Addressing environment's impact on human health

Financial Highlights

Total Revenue

$26.6bn

Strong revenue growth in FY2020 (9.2%)

- Helps the company gain investors' confidence.
- Helps to allocate funds for future growth prospects.

- **In 2020, Product Sales grew by 10% to $25,890 million.**

Reported operating profit

$5.2bn

Increase in the operational performance in FY2020 (76.5%)

- Can have great positive effects on growth and expansion plans of the company.
- Drastic turn-around from decreases experienced in 2017-2019

Financial Value and Risk

- **For the first time in several years, AstraZeneca is creating value at an acceptable level of financial risk**

AstraZeneca	2020	2019	2018
ROIC%	4.96	0.96	0.90
WACC%	2.28	5.66	8.93

- **Debt-to-Equity and Long-Term-Debt-to-Equity Ratios are showing annual improvements**
- **Current Ratio has exhibited little change**

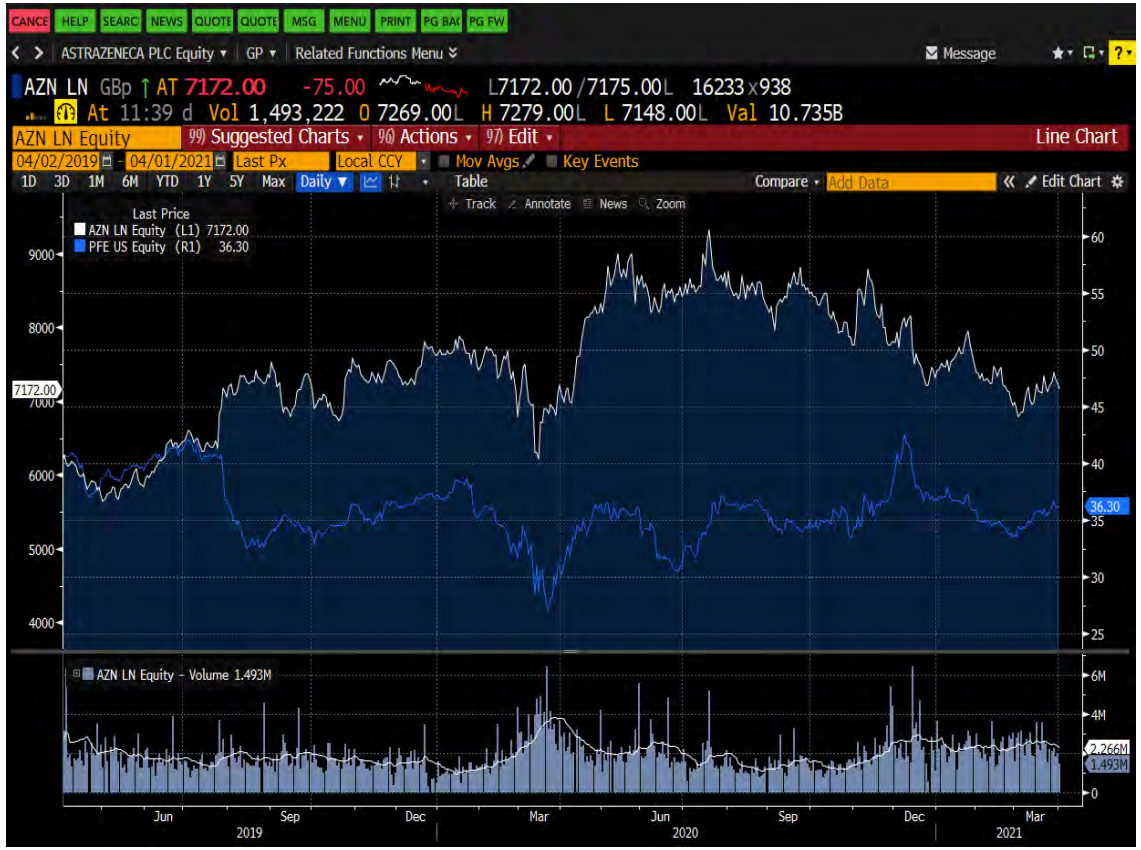
AstraZeneca	2020	2019	2018
Debt-to-Equity Ratio	1.3	1.4	1.5
Current Ratio	1	0.9	1
Long-Term-Debt-to-Equity Ratio	1.5	1.6	1.8

Peer Competitor Comparison

- All firms are creating value at an acceptable level of risk

Peer Comparison	AstraZeneca	Moderna	Pfizer
ROIC%	4.96	23.77	5.42
WACC%	2.28	10.2	4.46
Debt-to-Equity Ratio	1.3	0.05	0.61
Current Ratio	1	1.43	1.35
Long-Term-Debt-to-Equity Ratio	1.5	0.04	0.6

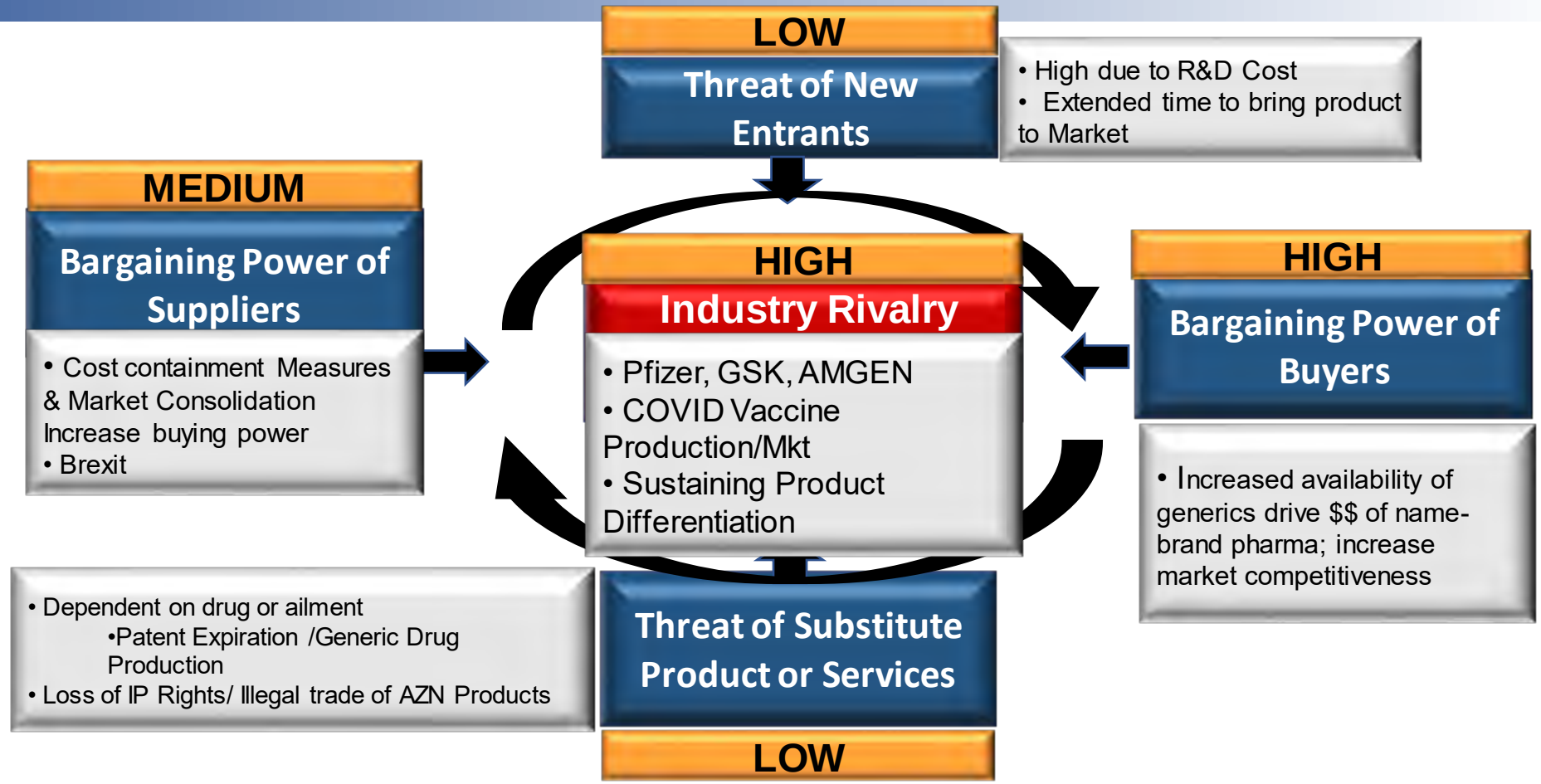
Peer Comparison: Pfizer & Moderna



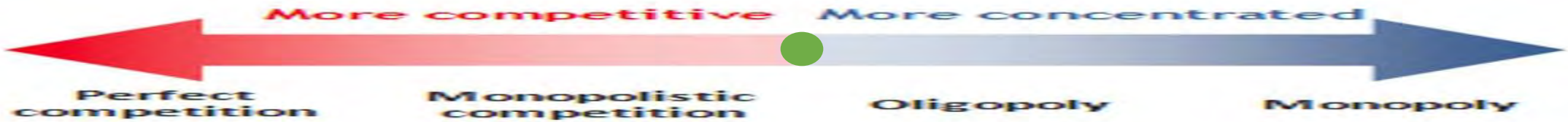
AZN VS PFIZER

AZN VS MODERNA

Porter's Five Forces Analysis



Competitive Spectrum



Supply Chain Management

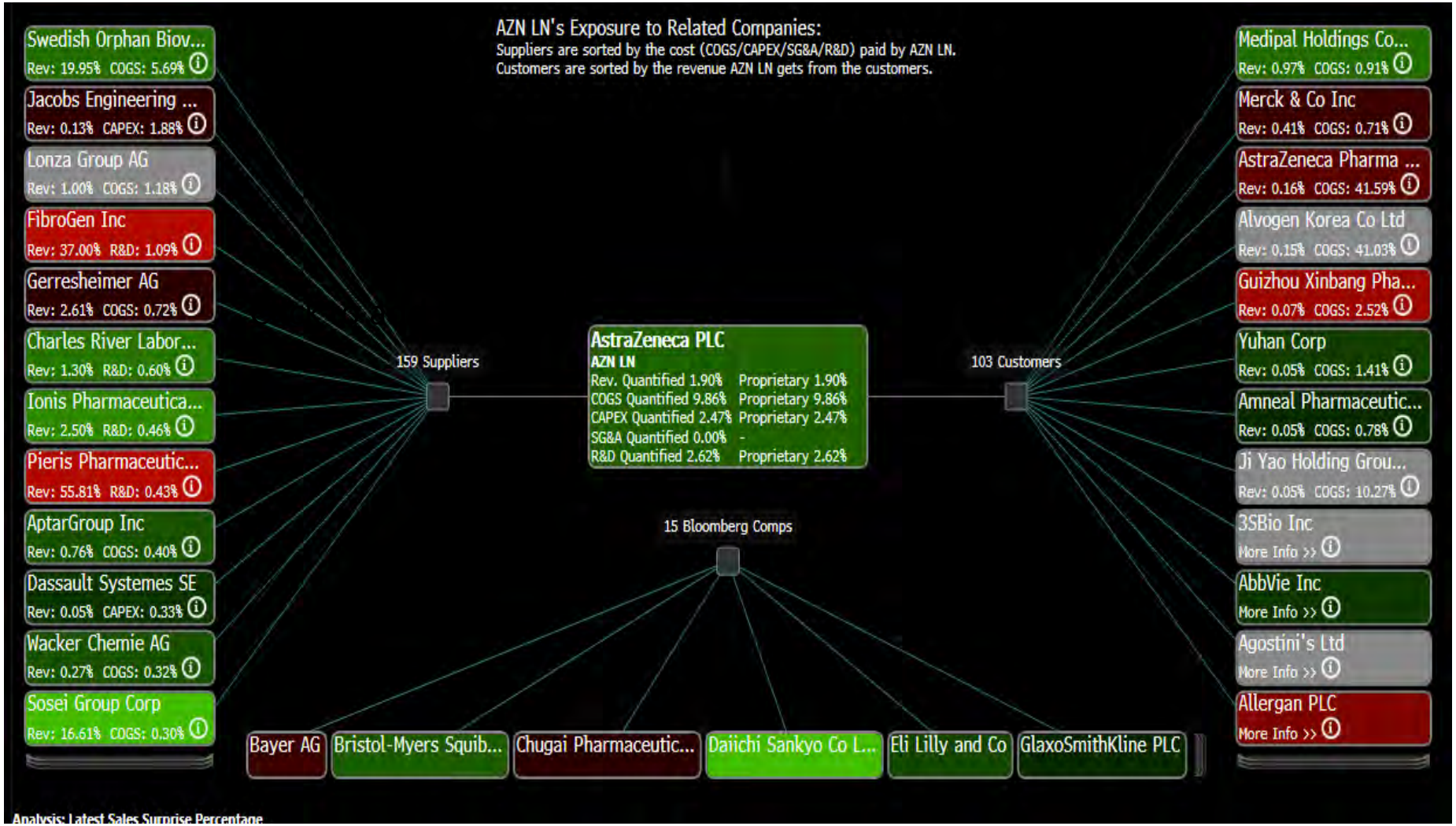
Supply Chain

159 Suppliers/303 Customers

Oncology/CVRM/R&I

Brexit Challenge

Storage Challenges
-Emergent Bio Lab

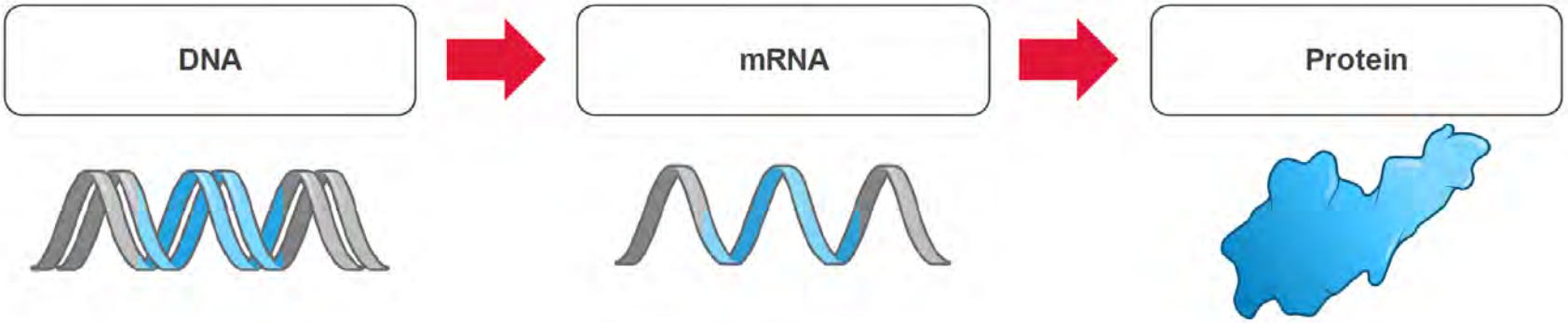


U.S. - Great Power Competition Recommendations

- National Security and Great Power Competition Implications
  - China's "Made in China 2025"
  - COVID-19 response

- U.S. Policy Recommendations
  - Reduction of contaminated pharmaceuticals importation to U.S. from China
  - Strengthening the U.S. industrial base and supply chain to minimize or mitigate the impacts of exogenous events (e.g., pandemics, natural disasters, etc.)
  - Strengthen information sharing networks with our strategic partners ensuring that entities from academia, industry, and government are integrated.

Firm Brief



Presenters

Maureen Farrell

Karl Painter

Jadee Purdy

Jason Schenck

Agenda

- **Industry Structure**
  - Moderna Profile/History
  - Ethical Concerns
  - Market Competition & Structure
- **Firm Conduct**
  - Porter's Five Forces
  - Strategic Game Board
  - Business Strategy
  - Innovation
  - Platform Technology
  - Risk Assessment
- **Firm Performance**
  - A Look at 2020/2021
  - Financial Analysis
  - Peer Competitor Comparison
- **USG Policy**
  - Global Health Threats
  - National Security Evaluation
  - USG Policy Recommendations

What will Moderna's story be…

Will Moderna be a one-hit wonder like Vanilla Ice or have twenty #1 hits and change the world like the Beatles?

or

?

Can mRNA help achieve U.S. National Interests?

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Industry Structure

Moderna Profile/History

- **Location:** Cambridge, Massachusetts
- **Key Subsidiaries:** 8 and growing
- **Employees:** 1,300
- **Founded:** 2011, ***founded and led by immigrants***, it was funded by Flagship Pioneering (biotech venture firm)/Noubar Afeyan-CEO and Chairman of Moderna's BoD
- **Key Leaders:** CEO: Stephane Bancel CTO: Juan Andres CMO: Tal Zaks, CFO: David Meline President: Stephen Hoge
- **Investors/Strategic Partners:** AstraZeneca, Merck, Alexion, Vertex, Bill & Melinda Gates Foundation
- **IPO:** December 2018 (raised $604.3 million in IPO of shares)
- **One Focus:** Messenger RNA (mRNA) therapeutics and vaccines leveraging a platform approach

Founding principle: The human body can be used to make its own medicine

Our mission

To deliver on the promise of mRNA science to create a new generation of transformative medicines for patients.

Ethical Concerns

- Balance speed with safety
- Decision about where to focus limited capacity next efforts: COVID variants or other illnesses
- Price point: profit versus accessibility
- Offered IP access during COVID pandemic
- Dr. Moncef Slaoui, former Moderna independent board member appointed to lead OWS – May 2020

Moderna as of February, 2021

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Pipeline

Commercial
COVID-19 vaccine

Phase 3 preparation
CMV vaccine

Phase 2
PCV, OX40L, VEGF

12 positive Phase 1 readouts
8 ID vaccines
PCV, OX40L, VEGF, anti-Chikungunya antibody (repeat dose)

Programs in development

Infectious Disease Vaccines

9 Vaccines for major unmet needs

- **COVID-19** launched
- **CMV** Positive Phase 2, Phase 3 preparation
- **hMPV/PIV3** Phase 1b age de-escalation study ongoing
- **RSV, Zika** in Phase 1
- **Flu, EBV, HIV and Nipah** in preclinical

mRNA Therapeutics

4 Therapeutic areas

- **5 Immuno-Oncology**: PCV, OX40L in Ph 2; Triplet, IL-12, KRAS in Ph 1
- **4 Rare Diseases**: PA open IND; MMA, PKU, GSD1a in preclinical
- **2 Cardiovascular Diseases**: VEGF in Phase 2; Relaxin in preclinical
- **2 Autoimmune Diseases**: IL-2 and PD-L1 in preclinical

Foundations

>1,300
Employees

6th
Consecutive year top employer by *Science*

Science 2020 TOP EMPLOYER

700 million to 1 billion
doses to be produced in 2021

8 commercial
subsidiaries across North America & Europe

$5.25B
of cash and investments (unaudited)[1]

Moderna's COVID-19 Vaccine: Authorized in 37 Countries

Received Emergency Use Authorization/conditional approvals

- United States (US FDA)
- Canada (Health Canada)
- **European Union (EMA/EC)**
- **United Kingdom (MHRA)**
- **Israel (MOH)**
- **Switzerland (Swissmedic)**
- **Singapore (HSA)**
- **Qatar (Ministry of Public Health)**

Started regulatory engagements with:

- World Health Organization
- Japan (PMDA)
- Taiwan (TFDA)
- Philippines (PH FDA)
- Indonesia (BPOM)

Deals signed[1]

- **United States** (300 million doses with option for additional 200 million doses)
- **European Union** (310 million doses with option for additional 150 million doses in 2022)[2]
- **Japan** (50 million doses)
- **Canada** (44 million doses)
- **South Korea** (40 million doses)
- **United Kingdom** (17 million doses)
- **Switzerland** (13.5 million doses)
- **Colombia** (10 million doses)
- **Israel** (6 million doses)
- **Taiwan** (5 million doses)
- **Qatar**
- **Singapore**

Market Structure & Competitive Spectrum

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Number of Firms: Many and growing

Barriers to entry: High

Number of buyers and sellers: Many buyers and sellers

Information: Information varies, but pretty good

Product Differentiation: Similar but slightly differentiated product

Efficiency: Firm produces at most efficient level

Translate BIO

BIONTECH

NOVAVAX

SANOFI

Pfizer

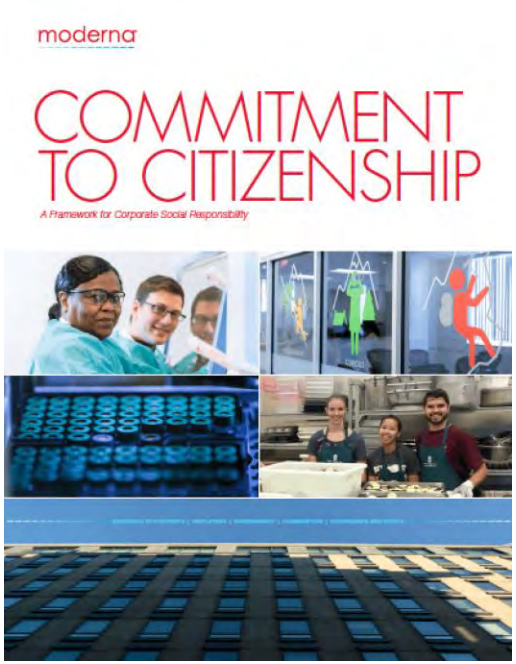
CUREVAC

the RNA people®

GILEAD

Johnson&Johnson

Firm Conduct



Porter's Five Forces

MODERATE

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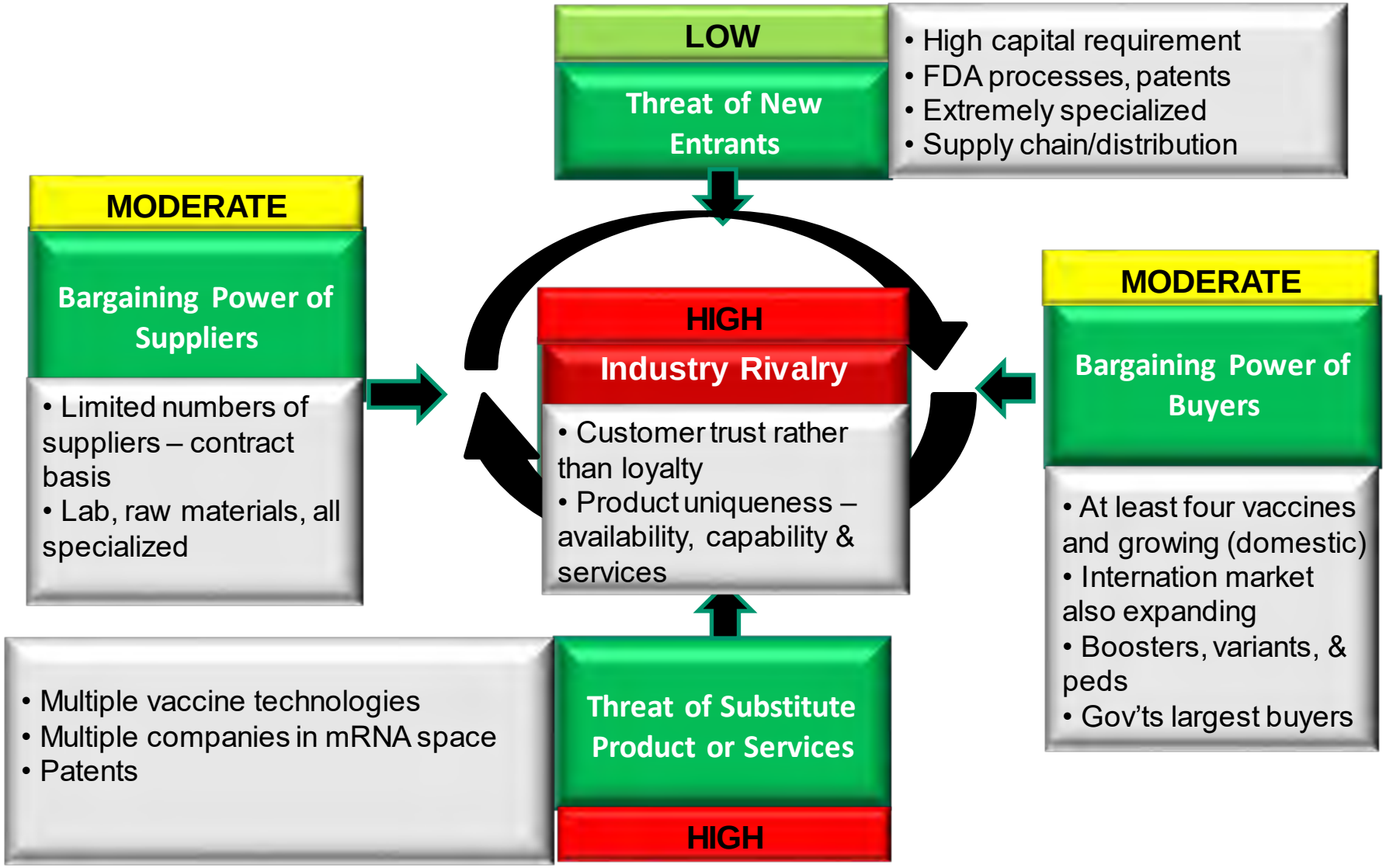


Strategic Game Board

Where

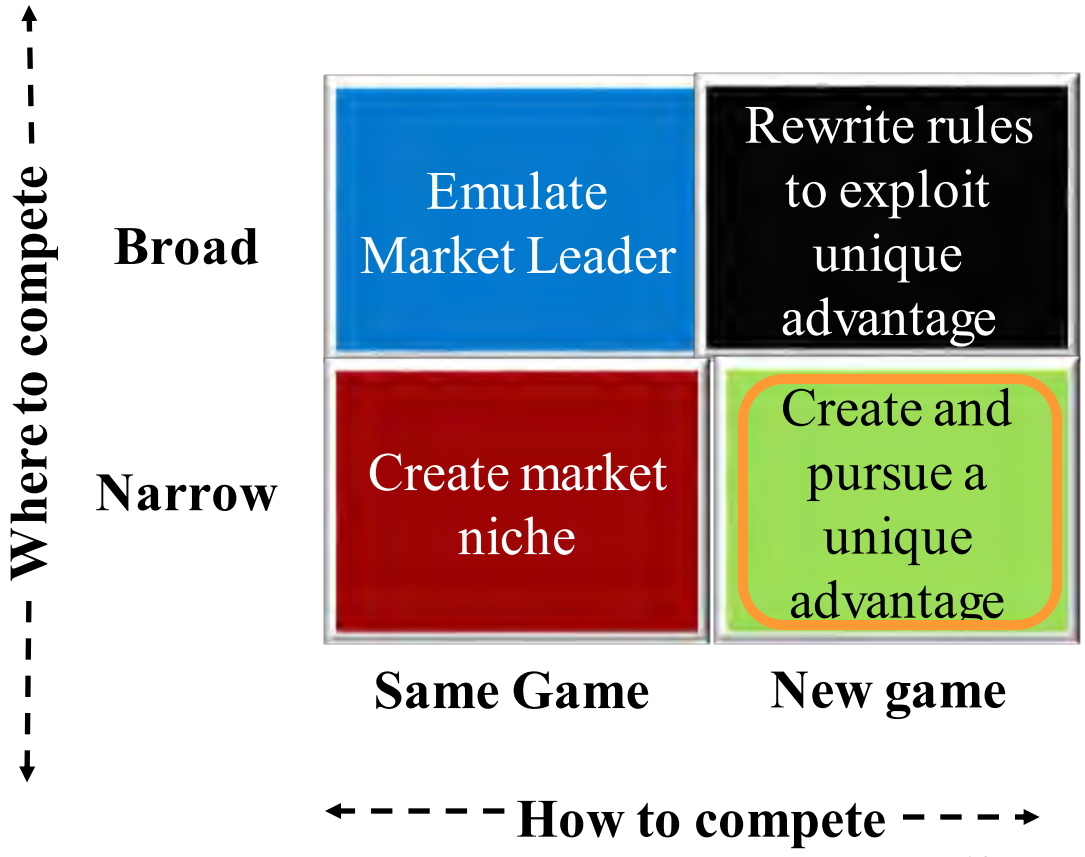
- Establishing a global footprint to manufacture and distribute vaccines and therapeutics quickly

How

- Execute better than rivals
- Build best in class manufacturing capabilities
- Continue pioneering in the mRNA space
- Patent Protection

When

- Continue technology platform investments
- Leverage capital to heavily invest in R&D
- Robust pipeline across modalities and add new ones



Business Strategy:
The Strategy Is What Moderna Says It Is

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#1 **Maximize the impact of Moderna COVID-19 Vaccine access**: manufacturing output for 2021, additional manufacturing capacity for 2022 and commitment to take variants of concern to the clinic

#2 **Accelerate vaccine development** to advance our pipeline and bring new vaccines to market

#3 **Generate human proof-of-concept data** in cardiovascular diseases, oncology and rare diseases

#4 **Continue to expand the use of mRNA technology** to maximize the potential impact we can have on patients; we continue to believe that Moderna will have, over time, many modalities with commercial products

By executing on these priorities, we will continue to advance our mission for patients and deliver value to our shareholders, our employees, our communities and our partners

This is just the beginning

Leading Innovation Supports Business Strategy

- Moderna is successfully leveraging current national innovation system dynamics and shifting priorities (BARDA engagement)
- Leading disruptive technology with mRNA
- Innovation is key to Moderna's business strategy
  - R&D: 3 new and 24 total development programs
  - Diversification in many different modalities
  - International expansion
  - Expanding production capability through partners
  - Minimal lobbying required due to current events

Moderna's Platform Technology

Biomedical platform as a source of value creation

Risk Assessment & Factors

Technology Risk - Inherent Risk Rating is High, Residual Risk Rating is **Moderate**
Biology Risk – Inherent Risk Rating is Moderate, Residual Risk Rating is **Low**
Execution Risk – Inherent Risk Rating is High, Residual Risk Rating in **Moderate**
Financing Risk - Rating is Low, Residual Risk Rating is **Low**

Overall Risk Rating = Moderate

Likelihood	**Severity**		
	Low	Moderate	High
Almost Certain		Execution Risk	
Possible	Biology Risk	Technology Risk	
Unlikely		Financing Risk	

Firm Performance

2020 Was a Historic Year

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January	July	December
Early-stage development company	Late-stage development company (with the start of our first Phase 3)	Commercial company

2019	2020
• No approved products • Negative cash flow from operations • Multiple capital raises needed to reach break even	• First product authorized/First product revenues • Q3 and Q4 positive cash flow from operations • Strong cash balance + cash generation

2020 demonstrated the power of harnessing mRNA to make medicines and showed the speed and scalability of the Moderna platform

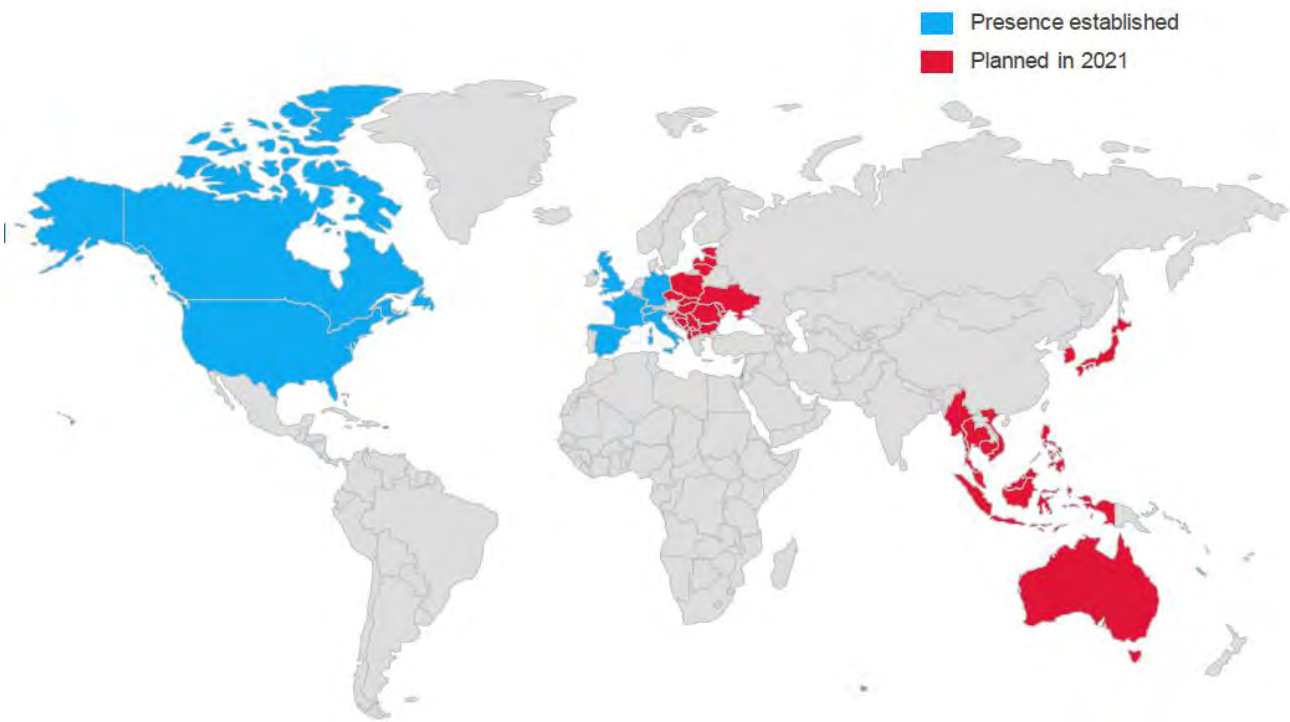
Moderna Expands Commercial Network Through New Subsidiaries and Partners 2020/2021

Completed 2020:

- Moderna USA
- Moderna Canada
- Europe
  - Moderna France
  - Moderna Germany
  - Moderna Italy
  - Moderna Spain
  - Moderna UK
  - Moderna Switzerland
- Israel (Partner: Medison)

Planned in 2021:

- Moderna Japan
- Moderna South Korea
- Moderna Australia
- Eastern Europe (distributor)
- ASEAN (distributor)



Value-Chain Vulnerabilities

- **Raw Materials (Lipids)**
- **Contracted Production**
- **Patent Disputes**
- **Lack of M&S Expertise**

Key Financial Information

(Amounts in $K)	2020	2019	
Revenue (Sales/Grants/Partnerships)	$ 803,395	$ 60,209	**Statement of Operations**
Operating Expenses	$1,566,539	$ 605,929	
Net Loss	**$ (747,064)**	**$ (514,021)**	
Cash & Cash Equivalents - End of Year	$2,635,935	$ 247,699	**Cash Flow Statement**
Total Assets	$7,336,750	$1,589,422	**Balance Sheet**
Total Liabilities	$4,775,375	$ 414,612	
Shareholder's Equity	$2,561,375	$1,174,810	
Effective Tax Rate	-0.30%	0.00%	

Financial Statements illustrate *rapid growth* of Firm

Revenue & Receivables

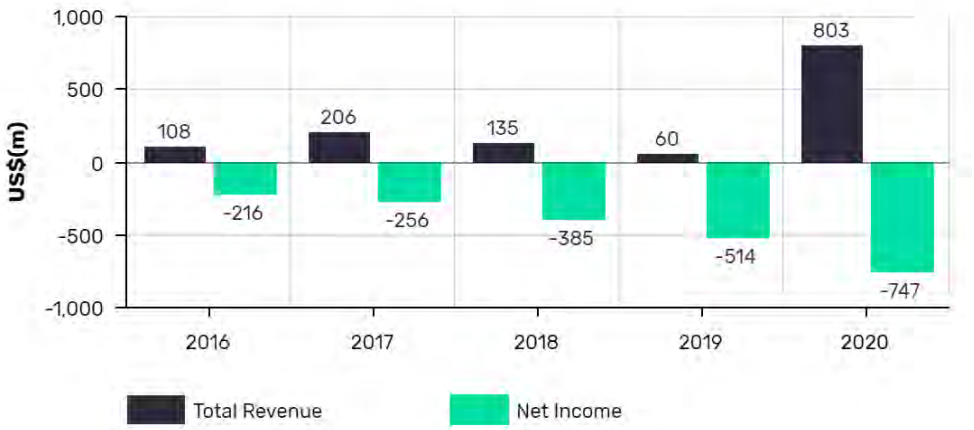
	Percentage of Revenue Years Ended December 31,			Percentage of Accounts Receivable December 31,	
	2020	2019	2018	2020	2019
Merck	*	61 %	49 %	*	13 %
BARDA	65 %	13 %	*	22 %	54 %
Vertex	*	10 %	*	*	17 %
AstraZeneca	*	*	34 %	*	*
U.S. Government (excluding BARDA)	24 %	*	*	*	*
European Commission	*	*	*	28 %	*
United Kingdom Government	*	*	*	11 %	*
South Korea Government	*	*	*	24 %	*

** - Represents an amount of less than 10%*

- 2020: USG largest revenue source (vaccine purchases/R&D grants)
- Merck/Vertex/AstraZeneca are R&D collaboration agreements
- Int'l revenue is unsecured & mostly vaccine sales
- Historical revenue was primarily from strategic alliances

We assess a *high probability* Accts Receivable will be collected

Value Creation/Financial Risk



	End 2020	Now
ROIC	-37.07%	23.77%
WACC	2.50%	10.20%
	ROIC < WACC	ROIC > WACC

	2020
Current Assets ($M)	$ 6,298
Current Liabilities ($M)	$ 4,389
Current Ratio	1.43

Long-Term Debt ($M)	$ 109.9
Shareholders Equity ($M)	$ 2,561.4
Long-Term Debt to Equity Ratio	0.04

Total Debt ($M)	$ 134.2
Total Shareholders Equity ($M)	$ 2,561.4
Debt to Equity Ratio	0.05

Our analysis indicates Moderna creates **Value** at an *acceptable level* of **Financial Risk**

Financial Risk (Peer Comparison)

MODERNA

	Most Current
ROIC	23.77%
WACC	10.20%
	ROIC > WACC

	2020
Current Assets ($M)	$ 6,298
Current Liabilities ($M)	$ 4,389
Current Ratio	1.43

Long-Term Debt ($M)	$ 109.9
Shareholders Equity ($M)	$ 2,561.4
Long-Term Debt to Equity Ratio	0.04

Total Debt ($M)	$ 134.2
Total Shareholders Equity ($M)	$ 2,561.4
Debt to Equity Ratio	0.05

BIONTECH

	Most Current
ROIC	5.93%
WACC	5.80%
	ROIC > WACC

	2020
Current Assets (€M)	1,091.8 €
Current Liabilities (€M)	268.5 €
Current Ratio	4.07

Long-Term Debt (€M)	€ 175.60
Shareholders Equity (€M)	€ 927.70
Long-Term Debt to Equity Ratio	0.19

Total Debt (€M)	€ 310.80
Total Shareholders Equity (€M)	€ 927.70
Debt to Equity Ratio	0.34

Both firms operating at *acceptable level* of **Financial Risk**

moderna

Recommended USG Policy

Global Health Threats

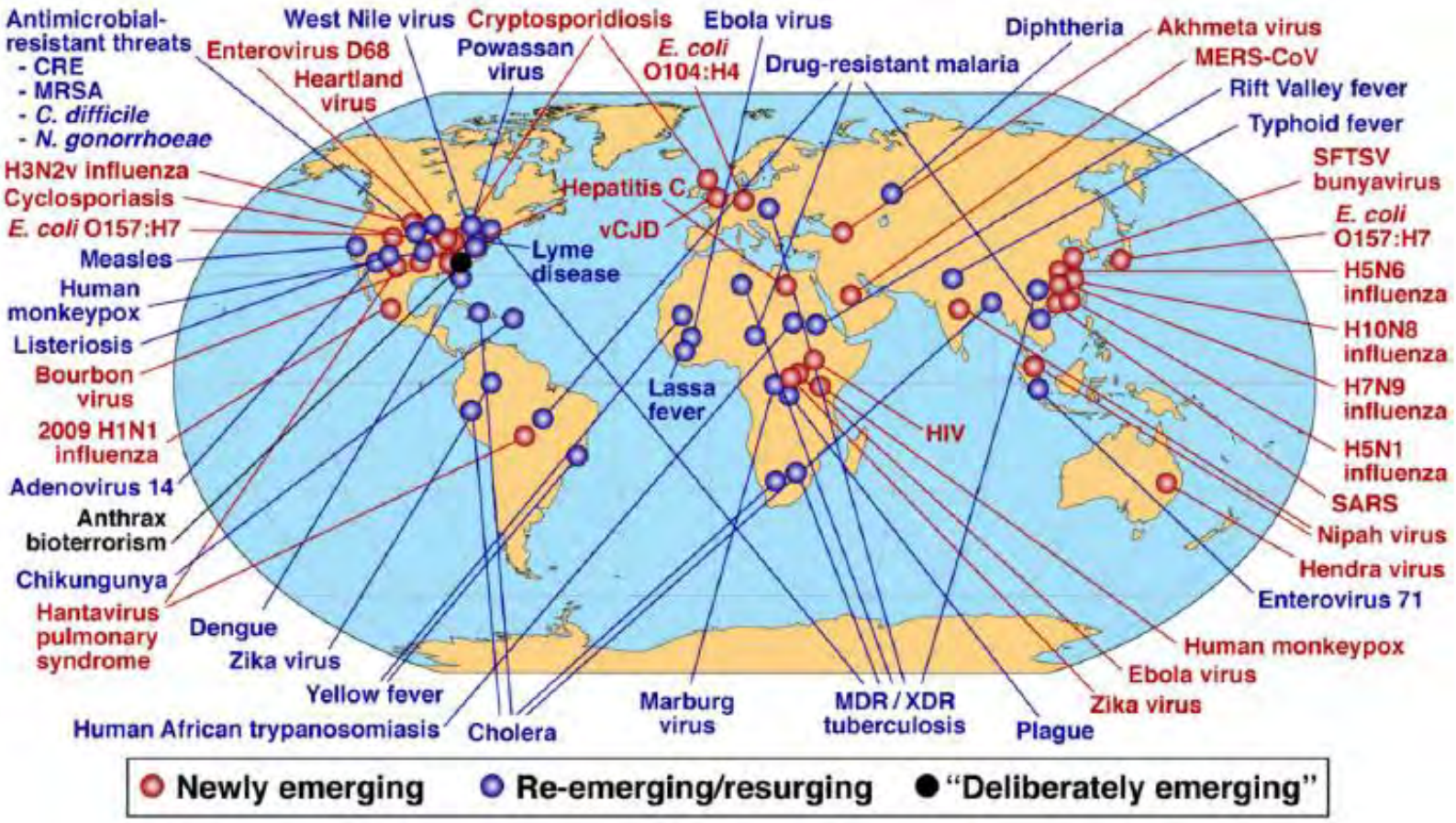


Figure 2: Global Examples of Emerging and Re-Emerging Infectious Diseases[11]

National Security Evaluation

- **Near-Term: Defeat COVID-19**
  - GPC – "Vaccine Diplomacy"
  - USG mobilized / Moderna operations surged
  - Reinvigorate allies & partners (readiness)
- **Long Term: Global Health Readiness**
  - Restore U.S. global health leadership
  - Leverage lessons learned from OWS
  - Protect against emerging health threats
  - Create/use capabilities for early detection and rapid response
  - Invest in STEM education & retain talent

Moderna is ready to deliver multiple #1 hits!

USG Policy Recommendations

moderna

1. **Procure/distro COVID-19 vaccines globally**
   - Leverages mobilized production capability & high-capacity utilization rate
   - Supports key pillar of NDS & GPC: "Vaccine Diplomacy"

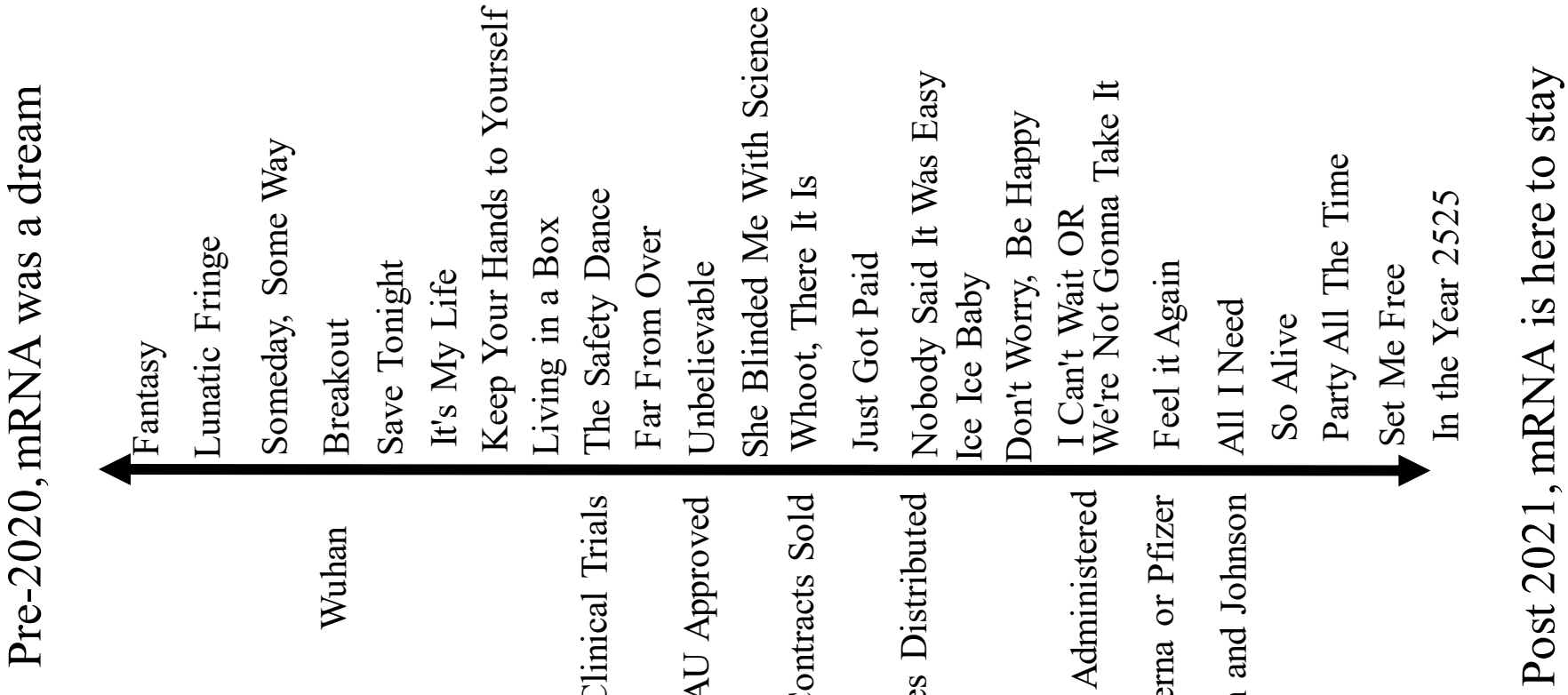
2. **Modify drug approval process based OWS lessons learned**
   - Opportunity to close "valley of death" for emerging drug treatments

3. **Invest in research on mRNA use for rare viruses**
   - Leverages "new class" of drugs & Moderna's parallel-development model
   - Addresses viral risks affecting DoD/DoS global footprint

4. **Invest in a global virus early-detection system**
   - Positions U.S. for rapid response during future health emergencies
   - Capitalizes on Moderna's ability to quickly formulate vaccines (2-3 weeks)

Questions/Guidance

Tale of Multiple One Hit Wonders



Russia and China GPC Context

- *America's Vaccine Diplomacy is AWOL in the Middle East* (Foreign Policy, 8 January 2021)
- *China and Russia are using coronavirus vaccines to expand their influence. The U.S. is on the sidelines.* (Washington Post, 24 Nov 2020)
- *Unable to get U.S. vaccines, world turns to Russia and China* (Politico, 25 Feb 2021).
  - China is shipping 1 million vaccines/ week to Africa
  - China has vaccinated 7 million Turks
- *Great Power Competition and the COVID-19 Vaccine Race. China, Russia, and the US are all using vaccines as diplomatic tools, giving a political dimension to other countries' medical choices.* (The Diplomat, 29 Jan 2021

Human Capital Issues/Efforts

- Departure of Chief Medical Officer (Dr.Tal Zaks)
- Hiring more staff to scale production / hiring globally
  - Grew from 830 (2019) to 1,300 (2020) employees
- Talent deficiencies in Support Activities
  - Marketing & Sales is most significant deficiency area
- High competition for human capital
  - 51% of employees: PhD, MD, JD, or Masters
- Rewards employees with equity (retention tool)
- Professional development training
- Moderna is known as a great employer
- USA Stem expertise gap

Moderna's Six Modalities

moderna

1. **Prophylactic Vaccines** (10) – COVID-19, Influenza, CMV, Zika etc.
2. **Cancer Vaccines** (2) – PCV (tumors), KRAS (CRC, NSCLS, pancreatic cancer)
3. **Intratumoral Immuno-Oncology** (3) (Solid tumors, lymphoma)
4. **Localized Regenerative Therapeutics** (1) Heart Disease
5. **Systemic Secreted & Cell Surface Therapeutics** (4) – Autoimmune, Heart Failure, Infectious Diseases, Rare Genetic Diseases
6. **Systemic Intracellular Therapeutics** (4)

ES Seminar 2 Firm Brief
Pfizer, Inc.

CDR Michael “Doc” Barna
CDR Thomas “Junior” Eisenstatt
Timothy Hale
LtCol Sarah Lenz
6 April 2021

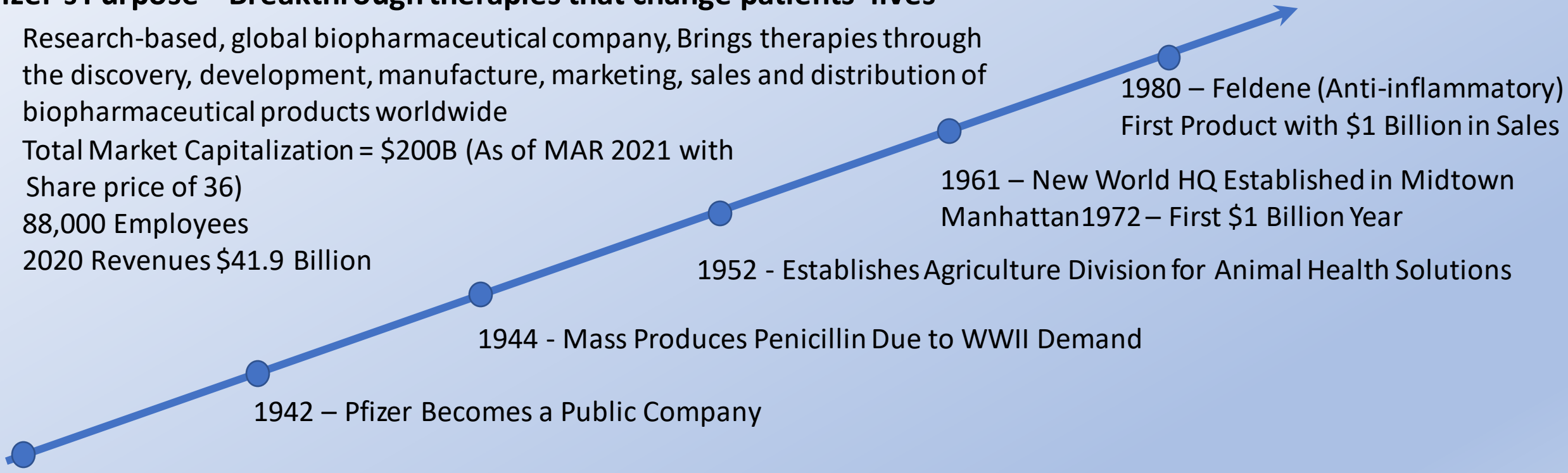
Agenda

- History
- Strategy
- Competition
- Value
- Strategy Discusssion

History

Pfizer's Purpose – Breakthrough therapies that change patients' lives

- Research-based, global biopharmaceutical company, Brings therapies through the discovery, development, manufacture, marketing, sales and distribution of biopharmaceutical products worldwide
- Total Market Capitalization = $200B (As of MAR 2021 with Share price of 36)
- 88,000 Employees
- 2020 Revenues $41.9 Billion



https://www.pfizer.com/people/history

Overall Firm Strategy

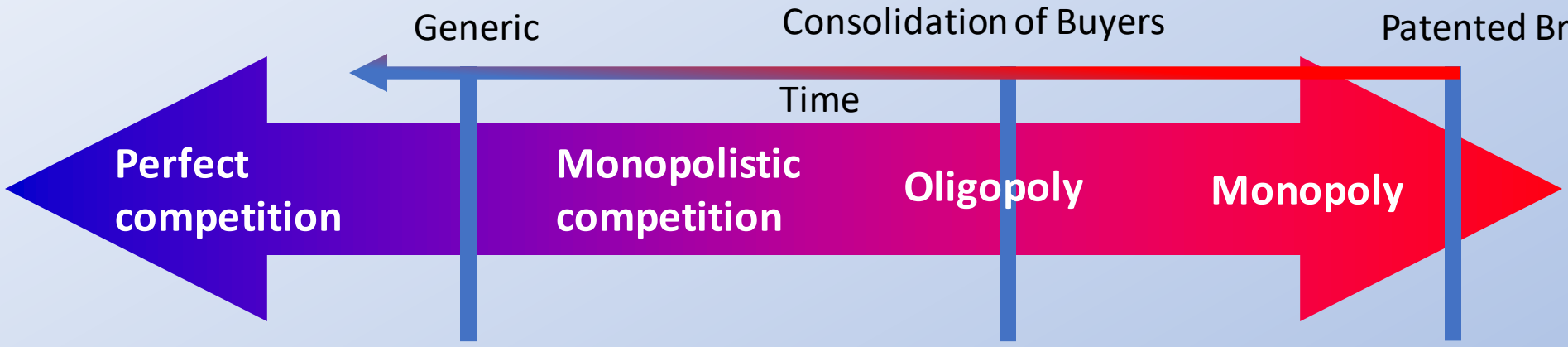
- Growth Strategy centered around 5 tenants
    1. Unleash the power of our people
    2. Deliver first-in-class science
    3. Transform our go-to-market model
    4. Win the digital race in pharma
    5. Lead the conversation

- Spun off its off-Brand Generic and Consumer Healthcare business sectors to focus on it's traditional role of being a science-based biopharmaceutical business on the discovery, development, manufacturing, marketing, sales and distribution of biopharmaceutical products world-wide

- Research and Development R&D is at the heart of fulfilling our purpose to deliver breakthroughs that change patients' lives

Why?
- Aging global population that is generating increased demand for innovative medicines and vaccines
- Advances in both biological science and digital technology that are enhancing the delivery of breakthrough new medicines and vaccines
- Increasingly significant role of hospitals in healthcare systems

The Competitive Spectrum



- Each company makes a similar product
- Still some barriers to entry (must still be able to make the generic). Hatch-Waxman Act lowered barriers
- Very Competitive

- Buyers become more defined with insurance companies and managed care organizations

- Large barriers to entry
- Patented, branded drugs can enjoy a monopolistic spectrum with:
- Many buyers and one seller
- However clock is ticking

Pharma Characteristics:
- intensely competitive and often highly regulated markets
- Competition includes; efficacy, safety, ease of use and cost

Porter's Five Forces

High: Medicare Part D and insurance companies

Medium: Multiple suppliers may decrease profitability

Low: Risky, expensive

Low: When drug is still under patent
High: Once patent expires

High: Intense competition for next "big" drug

Pfizer's Peer Competitors

https://www.investopedia.com/ask/answers/052015/who-are-pfizers-pfe-main-competitors.asp

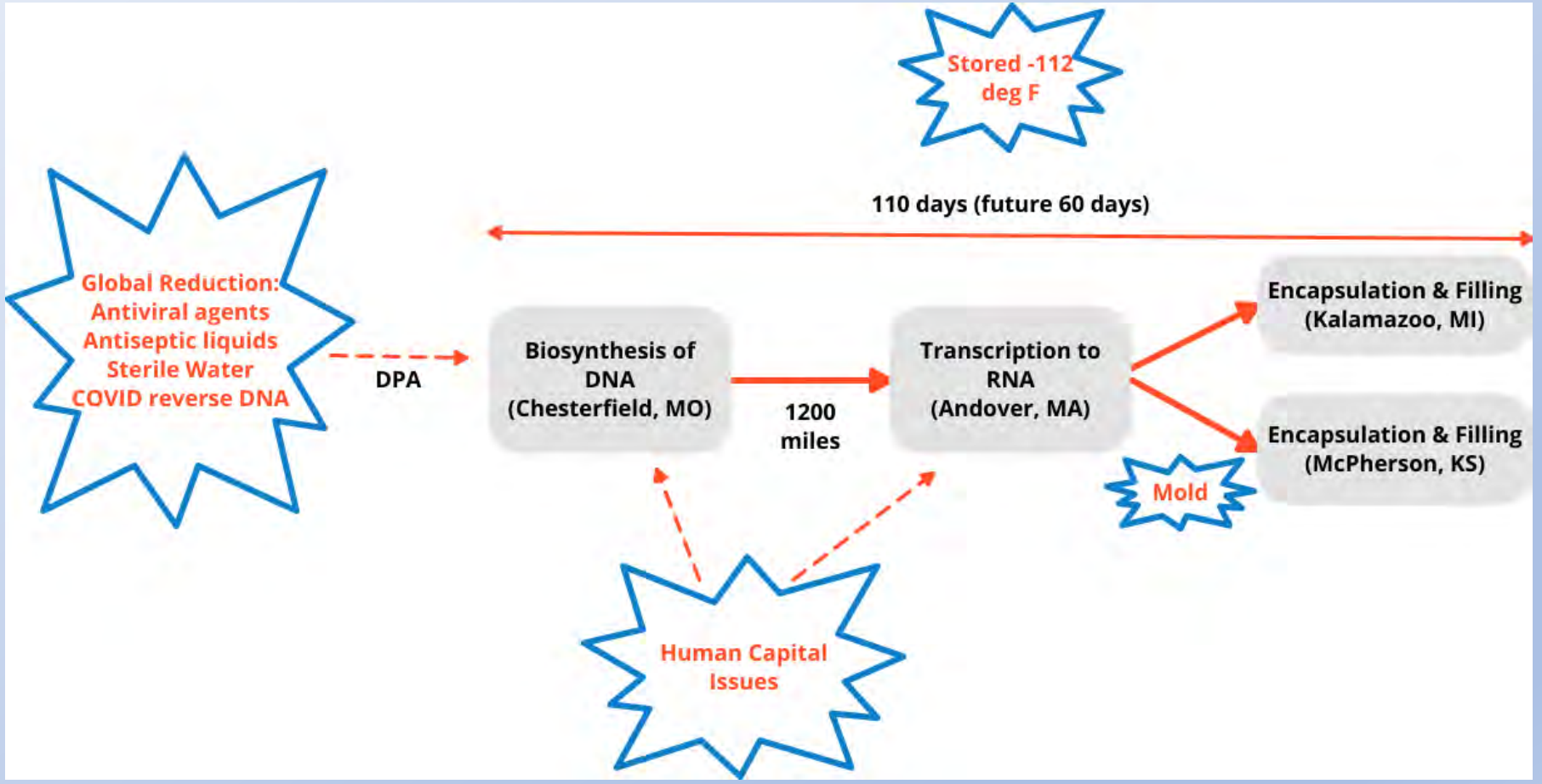
Pfizer's Strategy

Approaches to Innovation - "Bold Moves"

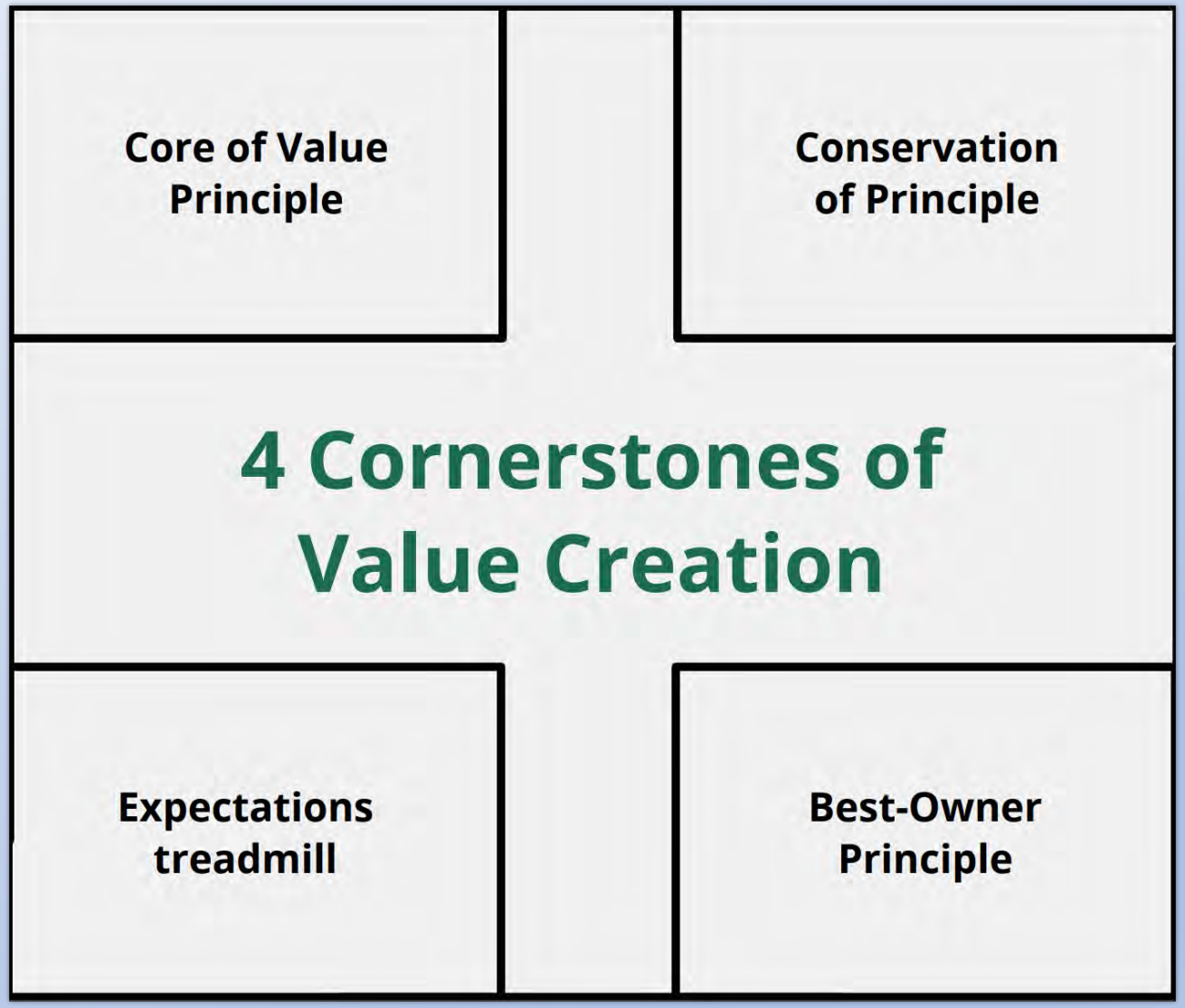
Unlease People Power	1st Class Science	Transform Go-To-Market	Win Digital Race	Lead Conversation
Diversity, Equity, and Inclusion Initiatives	Transformational products with 6 therapeutic areas	Promotion of biosimilars to drive value in healthcare	Digital Tools and Companions LiveWith App Mabu	Immunization for All Ages initiative
Performance and Insights leadership Program	Sourcing the best science through partnerships	Establishment of the Hospital Business Unit (HBU)	Automation and AI in clinical trial data system	4 Pillars for Patient Affordability
Global Fellowship Program	Portable Continuous Miniature Modular (PCMM) manufacturing	Global Health Innovation Grants	BMS Alliance & Fitbit NVAF	Rare Disease Research


Hey there, human buddy. What's cracking? Isn't that something people say?
Yup
I guess
I've never heard that

COVID-19 Supply Chain Issues



Value Creation



Core of Value Principle (ROIC>WACC)

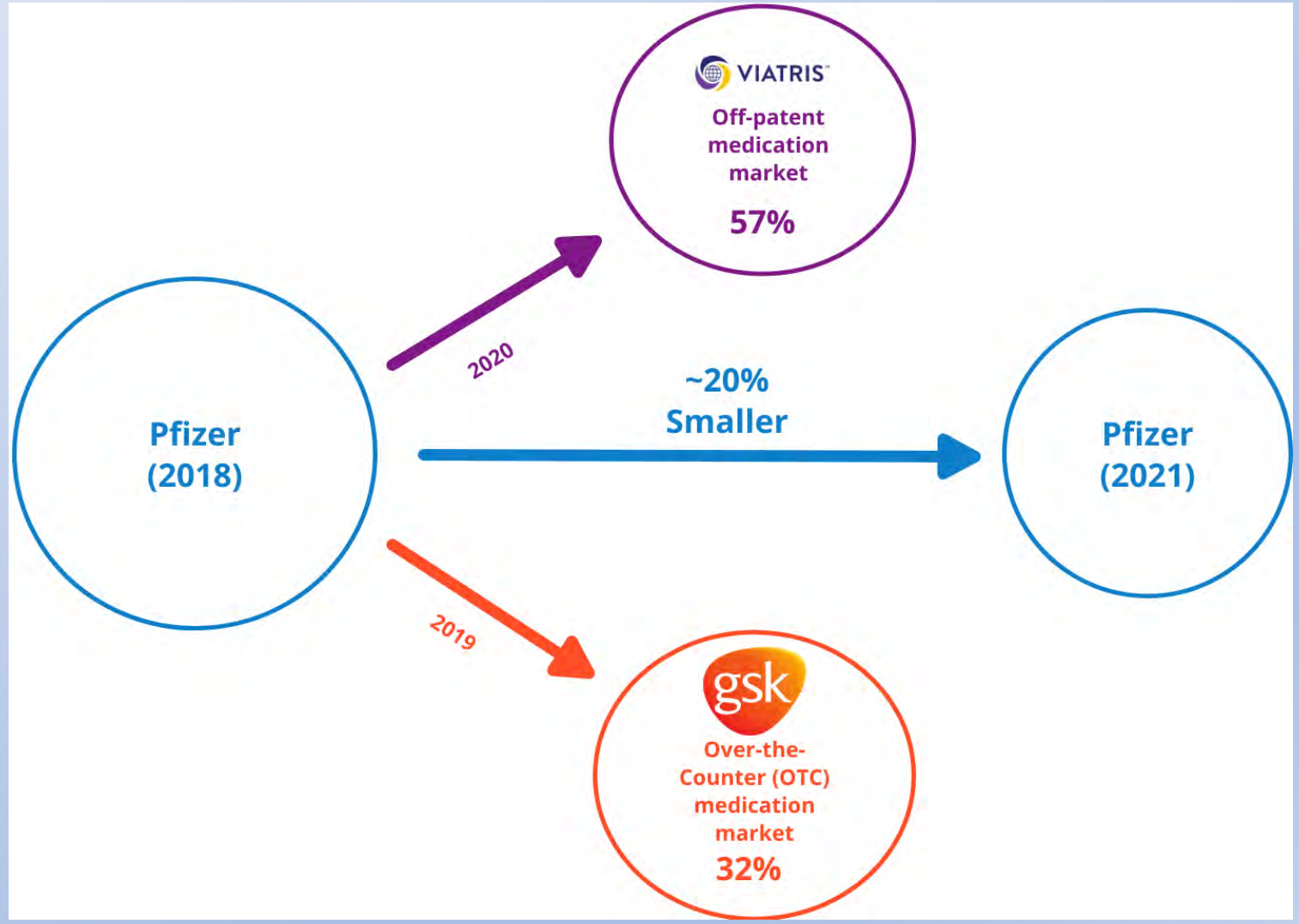
Companies create value by investing capital from investors to generate future cash lows at rates of return exceeding the cost of capital

ROIC > WACC

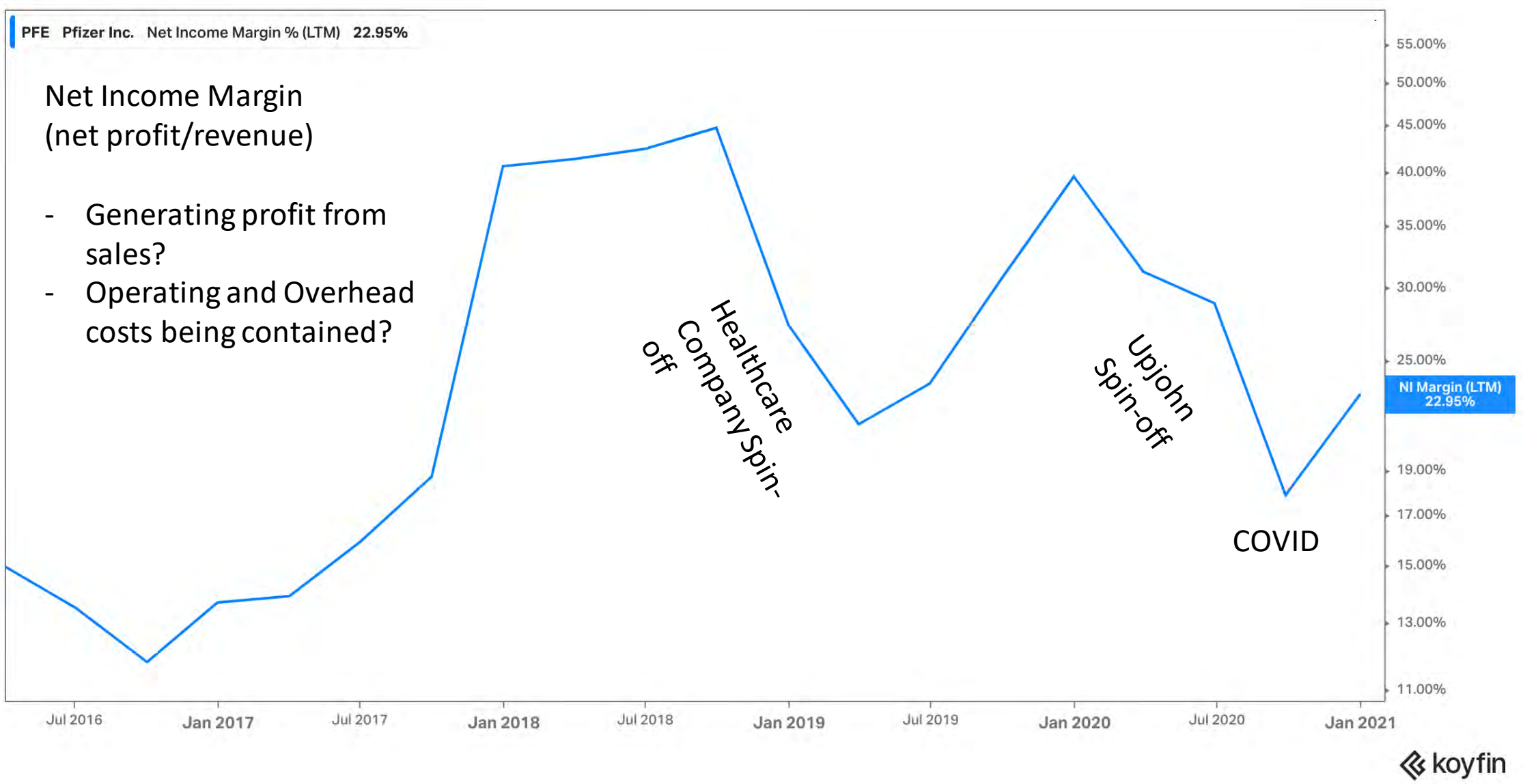
- 2020 – 5.87% vs 4.46%
- 2019 – 14.19% vs 4.05%
- 2018 – 11.81% vs 7.07%
- 2017 – (4.78%) vs 8.49
- 2016 – 6.18%. vs 7.35%

Conservation of Principle

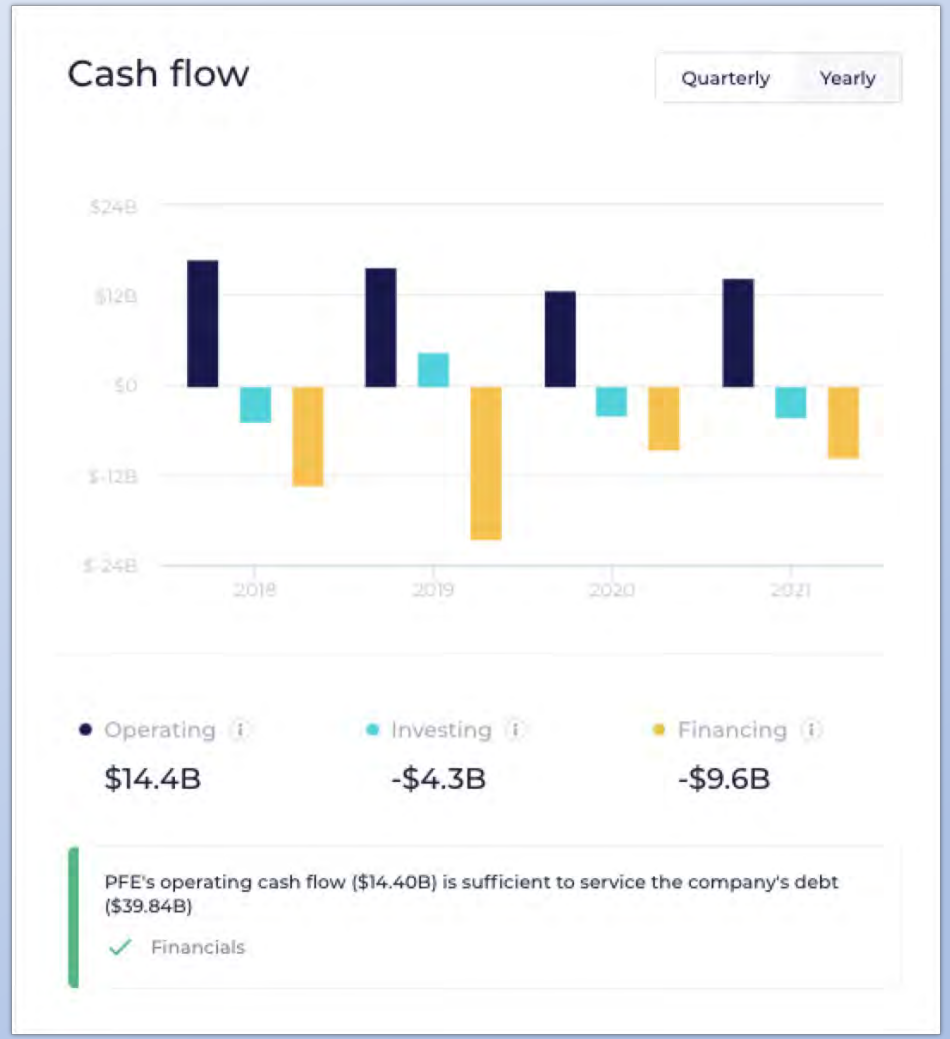
Value is created for shareholders when companies generate higher cash flows, not by rearranging investors claims on those cash flows



Conservation of Principle



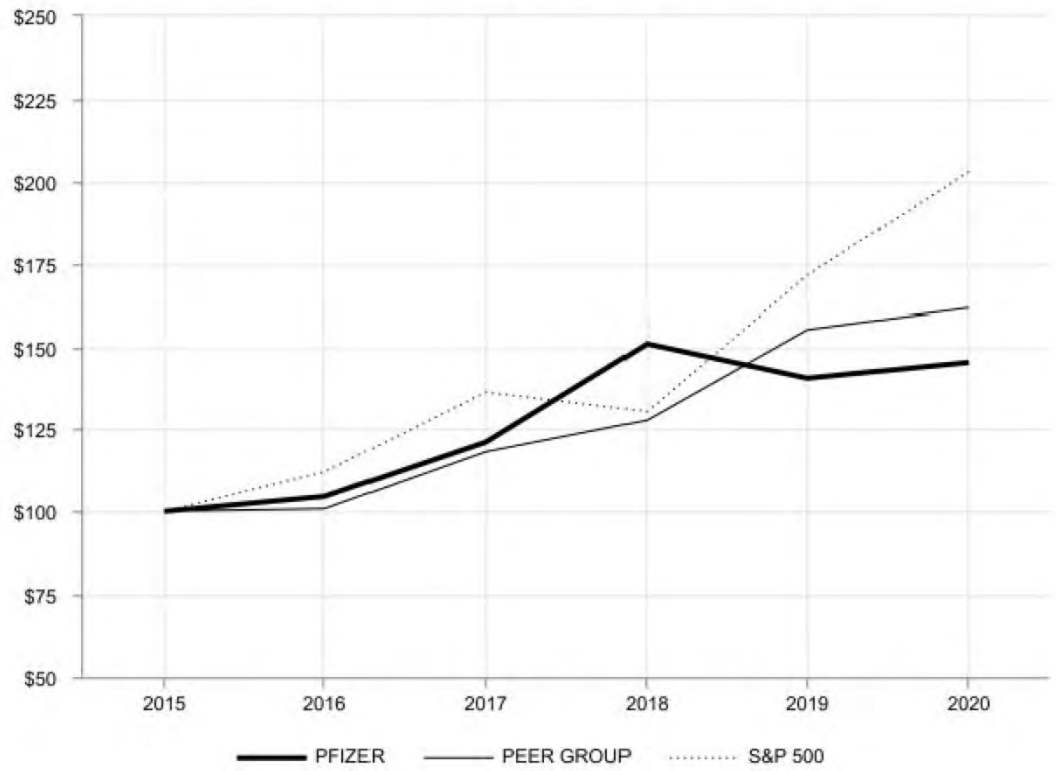
Cash Flow


Cash flow
Quarterly
Yearly
$24B
$12B
$0
$-12B
$-24B
2018
2019
2020
2021
Operating
$14.4B
Investing
-$4.3B
Financing
-$9.6B
PFE's operating cash flow ($14.40B) is sufficient to service the company's debt ($39.84B)
Financials

Pfizer vs Competition

PEER GROUP PERFORMANCE GRAPH

The following graph assumes a $100 investment on December 31, 2015, and reinvestment of all dividends, in each of the Company's Common Stock, the S&P 500 Index, and a composite peer group of the major U.S. and European-based pharmaceutical companies, which are: AbbVie Inc., Amgen Inc., AstraZeneca PLC, Bristol-Myers Squibb Company, Eli Lilly and Company, GlaxoSmithKline plc, Johnson & Johnson, Merck & Co., Inc., Novartis AG, Roche and Sanofi.



Five Year Performance

	2015	2016	2017	2018	2019	2020
PFIZER	$100.0	$104.5	$120.9	$151.0	$140.5	**$145.4**
PEER GROUP	$100.0	$100.8	$118.1	$127.8	$155.3	**$161.7**
S&P 500	$100.0	$112.0	$136.4	$130.4	$171.4	**$203.0**

Expectation's Treadmill

Stock market is driven by expectations of the future and not just current performance

Expectation's Treadmill

Our business includes the following therapeutic areas and key products:

Therapeutic Area	*Description*	*Key Products*
Internal Medicine	Includes innovative brands from two therapeutic areas, Cardiovascular Metabolic and Pain, as well as regional brands.	Eliquis*, Chantix/Champix* and the Premarin family
Oncology	Includes innovative oncology brands of biologics, small molecules, immunotherapies and biosimilars across a wide range of cancers.	Ibrance*, Xtandi*, Sutent*, Inlyta, Retacrit, Lorbrena and Braftovi
Hospital	Includes our global portfolio of sterile injectable and anti-infective medicines, as well as Pfizer CentreOne, our contract manufacturing and active pharmaceutical ingredient sales operation.	Sulperazon, Medrol, Zithromax, Vfend and Panzyga
Vaccines	Includes innovative vaccines across all ages—infants, adolescents and adults—in pneumococcal disease, meningococcal disease, tick-borne encephalitis and COVID-19, with a pipeline focus on infectious diseases with significant unmet medical need.	Prevnar 13/Prevenar 13 (pediatric/adult)*, Nimenrix, FSME/IMMUN-TicoVac, Trumenba and the Pfizer-BioNTech COVID-19 vaccine
Inflammation & Immunology	Includes innovative brands and biosimilars for chronic immune and inflammatory diseases.	Xeljanz*, Enbrel (outside the U.S. and Canada)*, Inflectra and Eucrisa/Staquis
Rare Disease	Includes innovative brands for a number of therapeutic areas with rare diseases, including amyloidosis, hemophilia and endocrine diseases.	Vyndaqel/Vyndamax*, BeneFIX and Genotropin

* Each of Prevnar 13/Prevenar 13, Ibrance, Eliquis, Xeljanz and Enbrel recorded direct product and/or Alliance revenues of more than $1 billion in 2020, 2019 and 2018. Each of Xtandi and Vyndaqel/Vyndamax recorded direct product and/or Alliance revenues of more than $1 billion in 2020, Chantix/Champix recorded direct product revenues of more than $1 billion in 2019 and 2018 and Sutent recorded direct product revenues of more than $1 billion in 2018. Eliquis includes Alliance revenues and direct sales.

For additional information on the key operational revenue drivers of our business, see the *Analysis of the Consolidated Statements of Income* section within MD&A. For a discussion of the risks associated with our dependence on certain of our major products, see the *Item 1A. Risk Factors—Concentration* section in this Form 10-K.

Patent Expiration

Based on current sales, and considering the competition with products sold by our competitors, the patent rights we consider most significant in relation to our business as a whole, together with the year in which the basic product patent expires, are as follows:

Drug	U.S. Basic Product Patent Expiration Year[1]	Major Europe Basic Product Patent Expiration Year[1]	Japan Basic Product Patent Expiration Year[1]
Chantix/Champix	2020[2]	2021	2022
Sutent	2021	2022	2024
Inlyta	2025	2025	2025
Xeljanz	2025	2028[3]	2025
Prevnar 13/Prevenar 13	2026	—[4]	2029
Eliquis[5]	2026	2026	2026
Ibrance	2027	2028	2028
Xtandi[6]	2027	*[6]	*[6]
Vyndaqel/Vyndamax	2024 (2028 pending PTE)	2026	2026
Xalkori	2029	2027	2028
Besponsa	2030	2028	2028[7]
Braftovi[8]	2031 (2031 pending PTE)	*[8]	*[8]
Mektovi[8]	2031[9]	*[8]	*[8]
Bavencio[10]	2033	2032	2033
Lorbrena	2033	2034	2036

Pipeline for New Drug Programs

Pfizer Pipeline Snapshot

Pfizer Pipeline Snapshot as of February 2, 2021

Pipeline represents progress of R&D programs as of February 2, 2021

- 14 programs advanced or are new
- 3 programs discontinued since last update
- Included are 64 NMEs, 31 additional indications, plus 0 biosimilar

Recent Approvals

- PF-06881894, a biosimilar to Neulasta®(1) (pegfilgrastim), is indicated in the treatment of Neutropenia in patients undergoing cancer chemotherapy (E.U.)
- BAVENCIO® (avelumab) for the maintenance treatment of patients with locally advanced or metastatic urothelial carcinoma that has not progressed with first-line platinum-containing chemotherapy (E.U.)

* PF-07302048 (Pfizer/BioNTech COVID-19 vaccine) received Emergency Use Authorization from FDA (U.S.) and conditional marketing authorization from the EMA (E.U.)

Pfizer Pipeline Snapshot as of October 27, 2020

Pipeline represents progress of R&D programs as of October 27, 2020

- 11 programs advanced or are new
- 7 program discontinued since last update
- Included are 58 NMEs, 33 additional indications, plus 1 biosimilar

Best-Owner Principle

- Albert Bourla - CEO
- William Carapezzi – Executive VP
- Frank A. D'Amelio - CFO
- Mikael Dolsten – Chief Science Officer

2017 – 2018 Pfizer Strategy Discussion

- Medicines provide significant value for both healthcare providers and patients
  - Improved treatment of diseases
  - Reduction in other healthcare costs: emergency room or hospitalization costs
  - Improvements in health, wellness and productivity.
- Actively engage in dialogues about the value of our medicines and how we can best work with patients, physicians and payers to prevent and treat disease and improve outcomes.
- Work within the current legal and pricing structures, as well as continue to review our pricing arrangements and contracting methods with payers, to maximize patient access and minimize any adverse impact on our revenues.
- We remain firmly committed to fulfilling our company's purpose of innovating to bring therapies to patients that extend and significantly improve their lives. By doing so, we expect to create value for the patients we serve and for our shareholders.

2019 Pfizer Strategy Discussion

- Medicines provide significant value for both healthcare providers and patients
  - Improved treatment of diseases
  - Reduction in other healthcare costs: emergency room or hospitalization costs
  - Improvements in health, wellness and productivity.
- Actively engage in dialogues about the value of our medicines and how we can best work with patients, physicians and payers to prevent and treat disease and improve outcomes.
- Work within the current legal and pricing structures, as well as continue to review our pricing arrangements and contracting methods with payers, to maximize patient access and minimize any adverse impact on our revenues.
- We remain firmly committed to fulfilling our company's purpose: ***Breakthroughs that change patients' lives.*** By doing so, we expect to create value for the patients we serve and for our shareholders.

2020 Pfizer Strategy Discussion

- ***Breakthroughs that change patients' lives.***
- 5 Bold Moves
  - Unleash the power of our people;
  - Deliver first-in-class science;
  - Transform our go-to-market model;
  - Win the digital race in pharma; and
  - Lead the conversation.

Human Capital

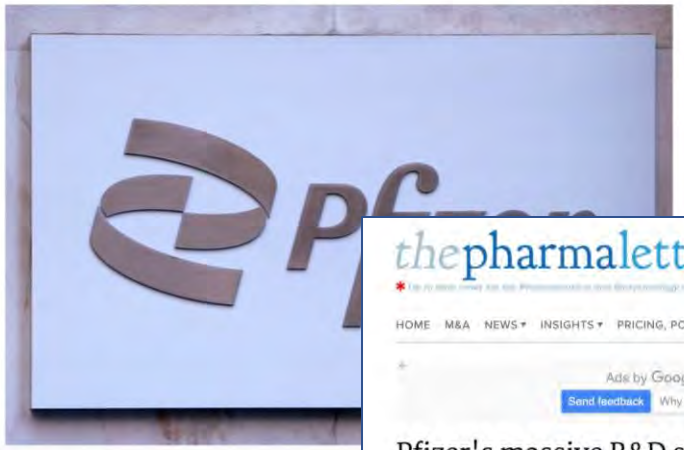
- Focus on Employee Growth and Development
  - Mentoring, Coaching, Development Plans
- Performance Based Pay
- Pfizer's Opportunity Parity strategy represents our commitment to increase diversity. In 2019, we announced representation goals, by 2025, of 47% for women (globally) and 25% minorities (US) for Vice President (VP) roles and above.
  - Representation of women at the VP level and above in 2019 was 34% globally (up 2% from 2018).
  - Representation of minorities in the U.S. at the VP level and above in 2019 was 20% (up 2% from 2018).

Activities

Pfizer to halt biosimilar output in China, sell assets to WuXi Biologics

By Reuters Staff 2 MIN READ

BEIJING (Reuters) - Pfizer Inc will stop producing biosimilar products in China and sell a unit in the eastern city of Hangzhou to WuXi Biologics Inc, the U.S. drugmaker said on Wednesday.



RACE FOR A CURE MARCH 17, 2020 / 2:10 AM / UPDATED A YEAR AGO

Pfizer, BioNTech to co-develop potential coronavirus vaccine

By Reuters Staff 2 MIN READ

(Reuters) - U.S. drugmaker Pfizer Inc PFE.N has signed a deal with Germany's BioNTech SE 22UAy.F to co-develop a potential vaccine for the coronavirus using BioNTech's mRNA-based drug development platform, the companies said on Tuesday.

BARRON'S

Topics Magazine Data Advisor Penta

BIOTECH AND PHARMA

Pfizer Drops the Big Blue Pill to Highlight Shift in Strategy

By Josh Nathan-Kazis Jan. 5, 2021 10:42 am ET

Text size

Courtesy Pfizer

Pfizer is dropping the big blue pill for something a bit more... science-y.

The pharma giant said Tuesday that it was adopting a new logo to replace the blue, pill-shaped oval that has represented the company since the late 1940s. The new symbol, also in blue, resembles a double helix, the shape of the DNA molecule.

The rebranding comes as Pfizer (ticker: PFE) completes a slimming-down that has seen it shed a range of businesses, to focus almost entirely on inventing and buying new

thepharmaletter

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Ads by Google Send feedback Why this ad?

Pfizer's massive R&D spend to continue as firm pledges unprecedented innovation drive

11-12-2006

Under the leadership of new chief executive Jeff Kindler, global drug giant Pfizer wants to revamp itself as a world-leading developer of original drugs. At its annual R&D day, which took place on November 30, the firm outlined bold new goals for innovation pledging that, by 2011 it will be producing four new drugs purely from in-house research. By 2010, it predicts that it will launch two new drugs a year via external collaborations.

"Our fundamental objective is to create a broad and very diversified stream of new products that will, year after year,

OTHER STORIES OF INTEREST

Advances in pharmacological treatment for amyloidosis
29-03-2021

Look back at pharma news in the week to March 26, 2021
28-03-2021

EMA's CHMP at last backs approving COVID-19 vaccines production plants
26-03-2021

EDITOR'S PICKS

Amazon: thr opportunity pharmaceuti

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The unique forum convening public and private sector leaders for networking, intelligence and debates on research and innovation.

More info

Most Read

1. The Horizon Papers
2. Israel, Switzerland and UK face exclusion from major EU quantum and space research projects
3. Official Horizon Europe work programmes now due in May
4. Horizon Europe draft work programmes

09 Jun 2020 | Network Updates | Update from Pfizer

These updates are republished press releases and communications from members of the Science|Business Network

Pfizer establishes new program to support continued biotechnology innovation

By Communication from Pfizer

Pfizer Inc. today announced the establishment of the Pfizer Breakthrough Growth Initiative, through which Pfizer will invest up to $500 million in biotechnology companies to help provide funding and access to Pfizer's scientific expertise to ensure continuity of the biotechnology companies' most promising clinical development programs.

"There has never been a more important moment to pursue new collaborations in our industry," said John Young, Pfizer's Chief Business Officer. "The Pfizer Breakthrough Growth Initiative seeks to do just this by injecting crucial capital into biotechnology companies that share our commitment to delivering transformative therapies for patients."

The Pfizer Breakthrough Growth Initiative will focus on making non-controlling equity investments in clinical-stage public companies, with a primary focus on companies with small- to medium-sized market capitalizations across a range of therapeutic categories that are consistent with Pfizer's core areas of focus: Internal Medicine, Inflammation & Immunology, Oncology, Rare Disease, Vaccines and Hospital. Partner companies may also have the opportunity to access Pfizer's significant expertise and resources in research, clinical development and manufacturing.

Today's announcement builds on Pfizer's long history of successfully collaborating across the healthcare innovation ecosystem, through a wide range of flexible partnering and funding models, with the shared goal of turning great science into innovative new medicines.

Biotechnology companies interested in learning more may contact pbgi@pfizer.com.

COVID-19 VAX Production Surge?

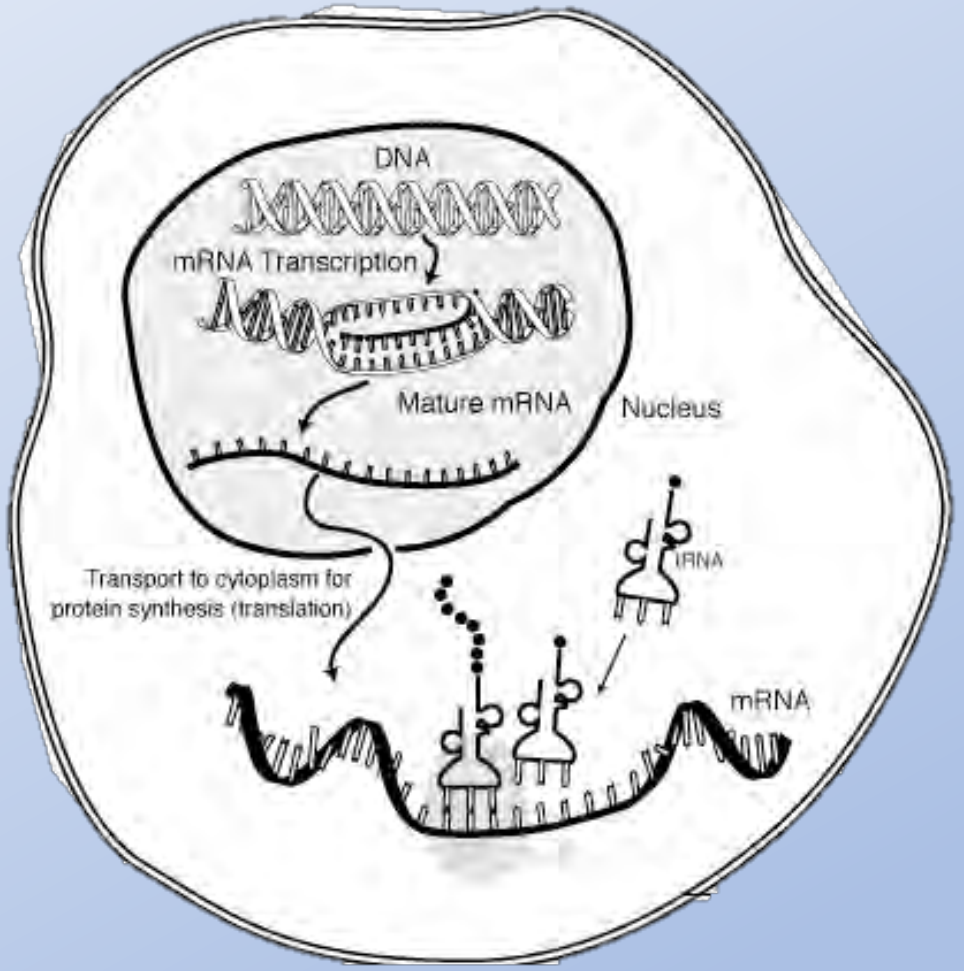
- Pfizer was unique in it's approach surging it's United States COVID production by re-prioritizing organic production capabilities.

- Many existing drugs that were pushed to the third party production facilities called Contract Manufacturing Organizations (CMOs) to make way for the Pfizer COVID Vaccine to be made in Pfizer owned facilities.

- Pfizer also produces the vaccine in multiple facilities in Europe with its German partner BioNtech.

- The U.S production capacity is planned to only be distributed to Americans. The European produced vaccine is planned to be sold to international countries and providers.

Questions


DNA
mRNA Transcription
Mature mRNA
Nucleus
Transport to cytoplasm for protein synthesis (translation)
tRNA
mRNA

Future regenerative therapies will demand higher performance and shorter recovery times.

Peter Battaglia
Gelson de Souza
Sampel Khouvilay
LTC Nadine K. Nally, USA

INTRODUCTION

01

Seek investors for R&D

02

Product Diversification

03

Partnerships

04

Attract Talent

05

Expand Business Opportunities

Theradaptive

Industry Structure	Firm Conduct	Firm and Industry Performance	USG Policy
• Five Forces • Competitive structure	• Strategic Game Board • Porter's Five Forces framework • Rumelt framework • Other strategy frameworks • Activity system • Balanced scorecard • Culture	• Firm financial analysis • NPV analysis • Other types of financial analysis (e.g., real option analysis) • Other types of qualitative analysis	• Policy menu • Policy choices from menu

PROFILE

"The idea for our work started in the back of a Humvee following an IED blast. The point was, how do you deliver a very targeted therapeutic to repair devastating injuries?"

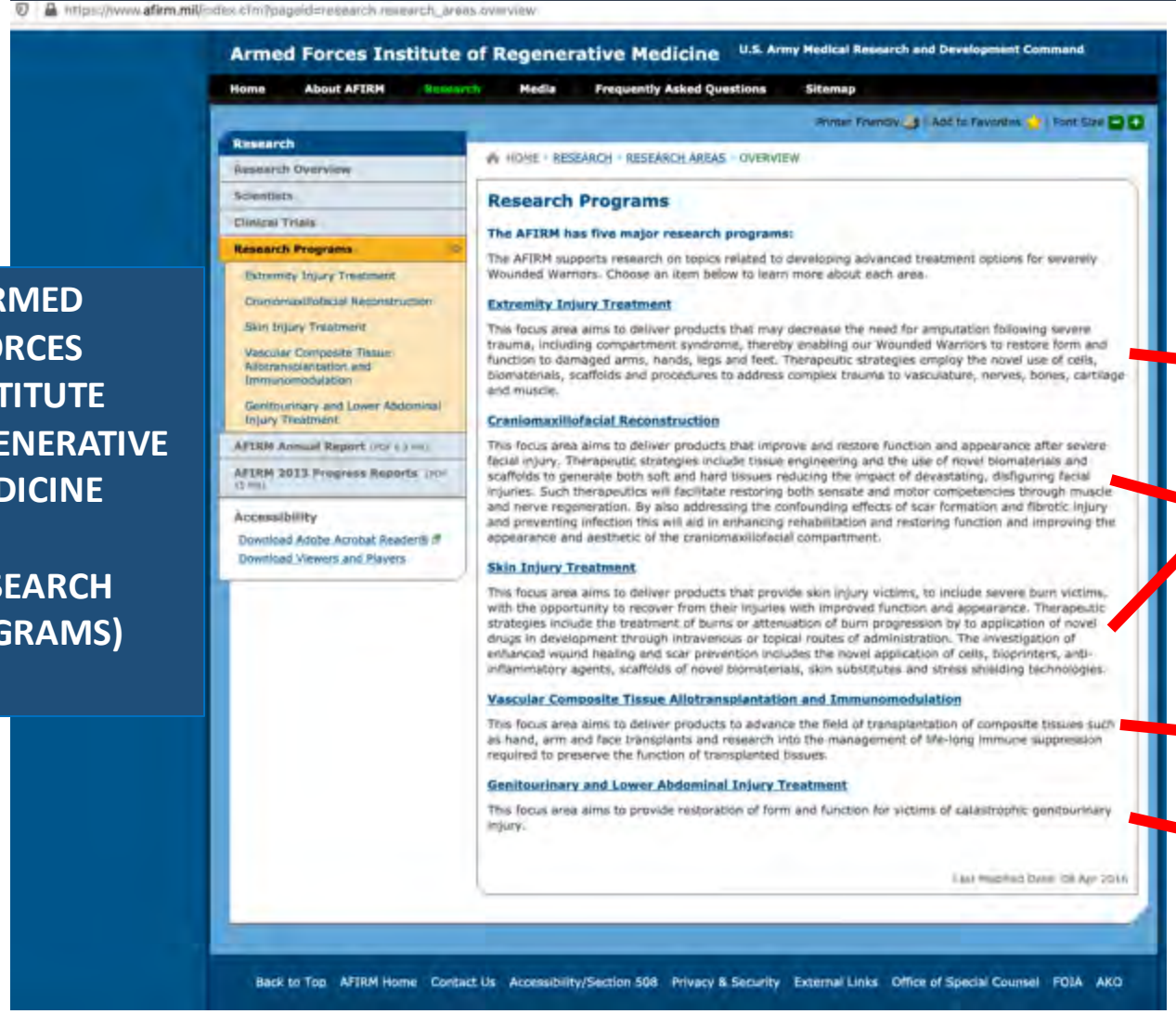
- **Founded:** 2016
- Location: Frederick, MD (**Frederick Innovative Technology Center (FITCI)**)
- Domain: Biotechnology platform in regenerative medicine (Private)
- **Key Leader**: Founder/CEO, Dr. Luis Alvarez
- **Employees: 10**
- **Focus:**
  - **MIT spin-out developing a biologics delivery platform for orthopedic regeneration.**
  - Raising funds to Clinical Trials (U.S., Europe and South America)
  - Spinal fusion and trauma is an increasing market with huge competition (**substitute risk**).
  - Recombinant protein is a method ethically accepted.
- **Partnerships:** OrthoRebirth
- **Potential Partners:** (Medtronic, Stryker, AlloSourcé, DePuySynthes).
- **Investors: 4**

***Future**: DoD and Veterans Affairs are interested in bringing to market a product that can improve the treatment for active and retired military (Human Capital).*

THERADAPTIVE PORTFOLIO

ARMED FORCES INSTITUTE OF REGENERATIVE MEDICINE

(RESEARCH PROGRAMS)



FOCUS AREAS
SKIN REGENERATION
EXTREMITY REGENERATION
CRANIOMAXILLO-FACIAL RECONSTRUCTION
VASCULARIZED ALLOTRANSPLANTATION & IMMUNOMODULATION
GENITOURINARY AND LOWER ABDOMEN INJURY

Theradaptive Porfolio meets AFIRM Research Programs
ALTRUIST (MILITARY INSPIRATION) or BUSINESS VIEW ?

MARKET / PRODUCT

PRODUCT

Orthopedic Biomaterial ($80B global market)

Market Growth Rate: 10%

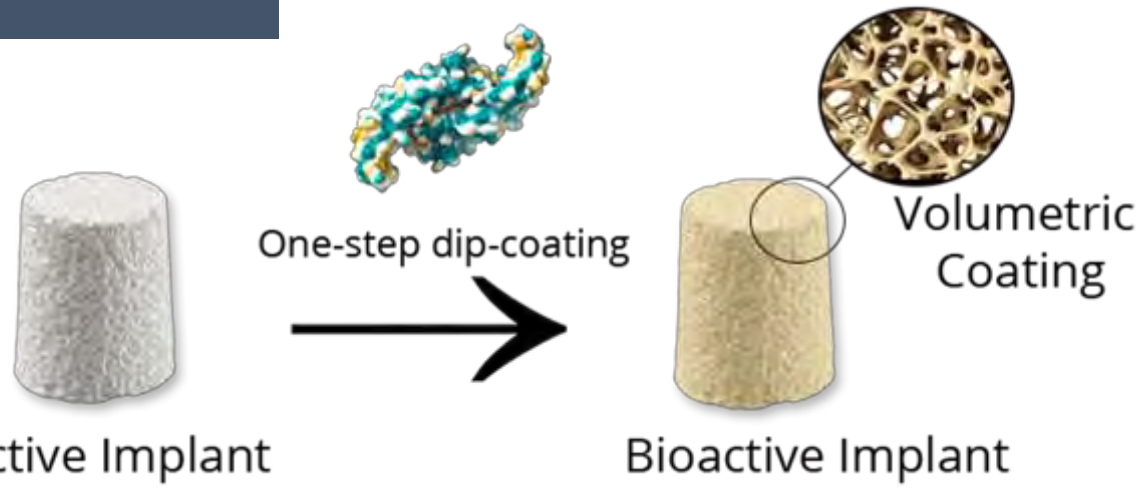
BMP2 vs AMP2

APPLICATION

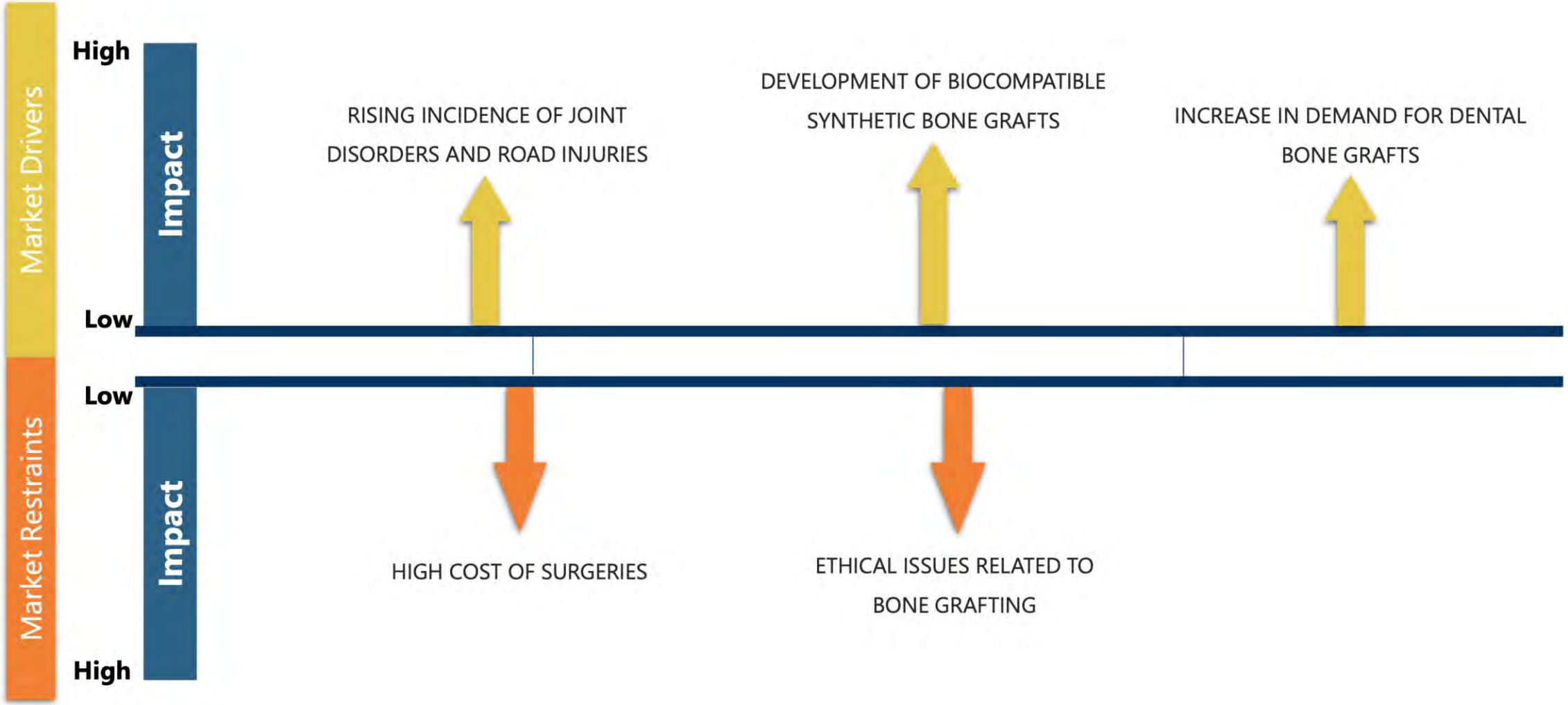
- Spinal Fusion
- Long Bone Repair
- Dental & Facial Bone Repair
- Osteochondral Repair

One Product entering Clinical Trials

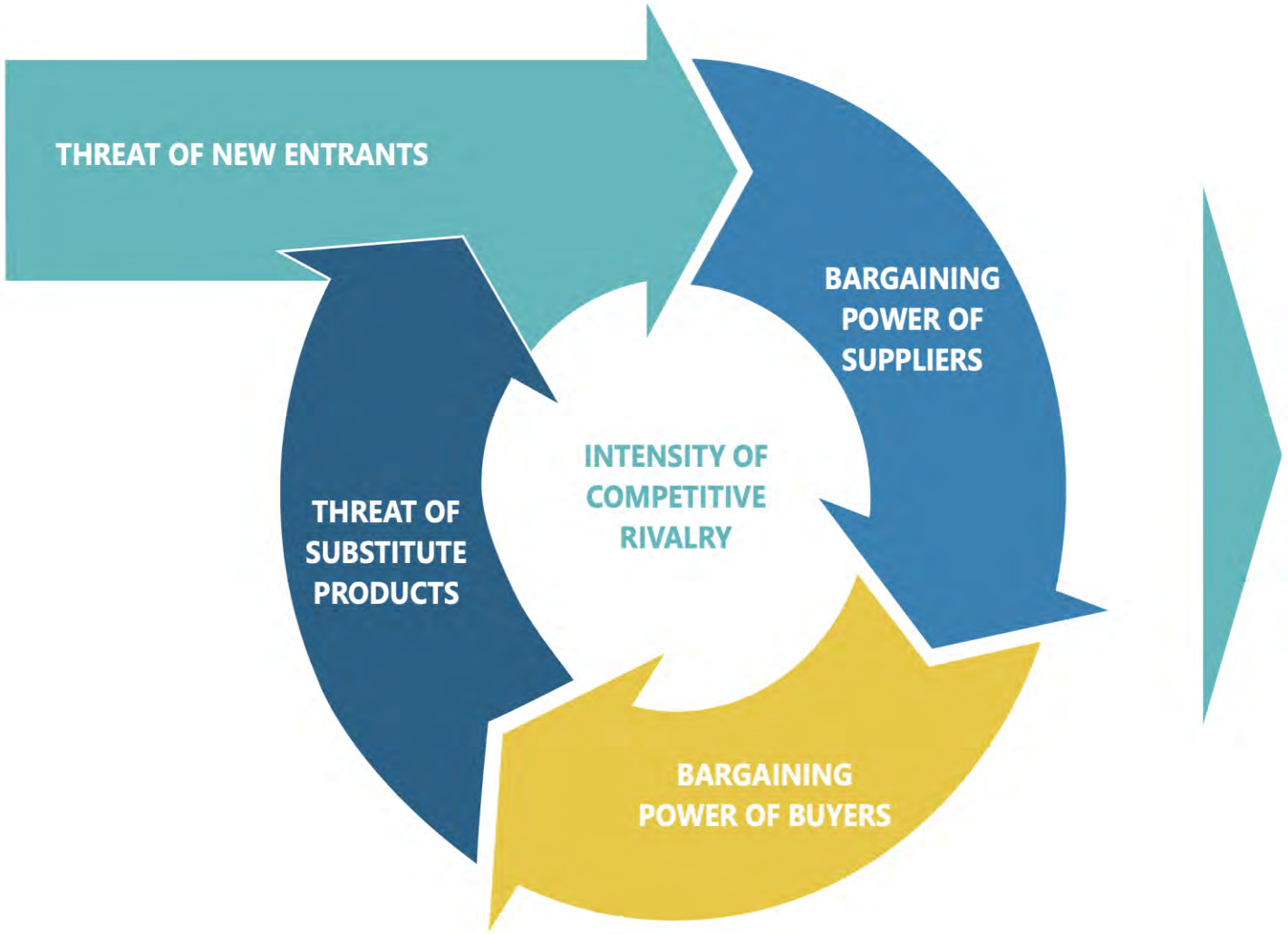
A platform for technology



MARKET DYNAMICS



MARKET STRUCTURE / RELEVANT FORCES



RELEVANT FORCES

The intensity of **competitive rivalry** is likely to be **moderate**, over the forecast period.

The **threat of substitute products** is likely to be **moderate high**, during the forecast period.

MARKET RIVALRY

SPINE FUSION END BONE REPAIR APPLICATION

Medtronic

stryker

DePuy Synthes
PART OF THE Johnson & Johnson FAMILY OF COMPANIES

ORTHO ReBIRTH

ZIMMER BIOMET

RIVALRY AMONG COMPETITORS (RISKS)

BMP-2

AMP-2

BMP-2, like other bone morphogenetic proteins, plays an important role in the development of bone and cartilage.

Vs.

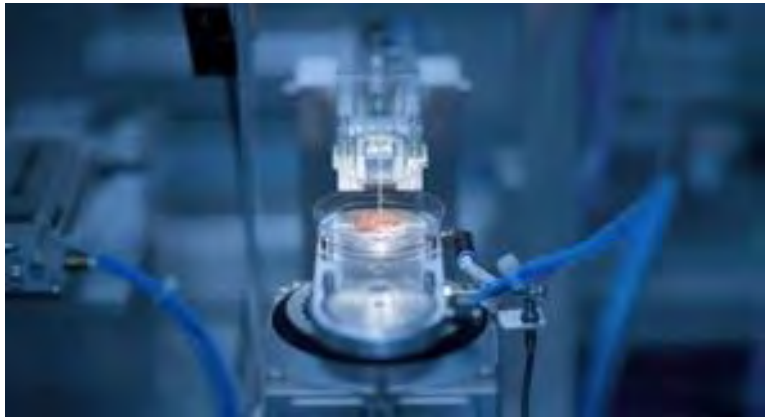
AMP2 protein is a proprietary variant **of BMP2, which is the most potent bone-forming therapeutic currently used in humans. AMP2 could capture a significant portion of the $8 billion US spinal fusion market**.

THREAT OF SUBSTITUTES RISK

Technologies and products registered in Russia by the end of 2011 to correct tissue defects.

Disease/Tissue to Be Restored	Source of the Cells	Matrix
skin and other tissues	allogenic and autologous fibroblasts	– *
skin and other tissues	dermal fibroblasts	collagen I/fibrinogen
heart muscle	autologous bone marrow MSCs differentiated into cardiomyoblasts	
bone defects of the upper and lower jaw	autologous MSCs differentiated in osteogenic direction	matrix
cartilage tissue	autologous chondroblasts	three-dimensional gelatine matrix
chronic lower limb ischemia	MSCs	– *
recessions and mucosal deficiency in the area of teeth and dental implants	fibroblasts of the oral mucosa	– *
ulcerative colitis and Crohn's disease	MSCs	– *
tuberculosis	MSCs	– *

* These hyphens mean that in these products no matrix was used.



Theradaptive

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REGENERATIVE MEDICINE PRODUCT DEVELOPMENT

AMP2/ THX-14

BIGPHARMA ACQUISITION PROPOSAL

Product Discovery | Preclinical | Clinical Trials | FDA Review | Scale-Up to Mfg./Phase IV | Post-Marketing Surveillance

PRE-DISCOVERY

BASIC IDEAS

Cells
Devices
Biologics
Drugs
Combination

150+ Products

BENCHTOP

50 Products

ANIMAL

IND, IDE SUBMITTED

17 Products

PHASE 1 10-20 Volunteers

PHASE 2 50-100 Volunteers

PHASE 3 100-200 Volunteers

HUMANS

20-100

100-500

1,000-5,000

NDA SUBMITTED

ONE FDA-APPROVED DRUG

3 – 7 Yr | .5 – 2 Yr | 1 – 2 Yr | 2 – 3.5 Yr | 2.5 – 4 Yr | 1 – 2 YEARS | INDEFINITE

$100-130M | $60-70M | $60-100M | $130-160M | $190-220M | $18 -20M

ESTIMMATED: $568-700 M per Drug and 10-20.5 years

Sources:

- *Mullin, R., "Cost to Develop New Pharmaceutical Drug Now Exceeds $2.5B", https://www.scientificamerican.com/article/cost- to-develop-new-pharmaceutical-drug-now-exceeds-2-5b/*
- *Guest Speaker, February 2021.*

STRATEGIC GAME BOARD

REGENERATIVE MEDICINE MARKET

Where to compete

	Same game (traditional rules)	New game (rewrite rules)
Across-the-board (entire market)	**Emulate market leader's functional approach, strengths**	**Rewrite industry rules to exploit a unique, industry-wide advantage**
Selective (market niche)	**Resegment the market to create a niche**	**Create and pursue a unique advantage**

How to compete

"Redefine regenerative field."

"No singular molecules."

"Implants like paint, making them more readily available for cells on the body to interact with."

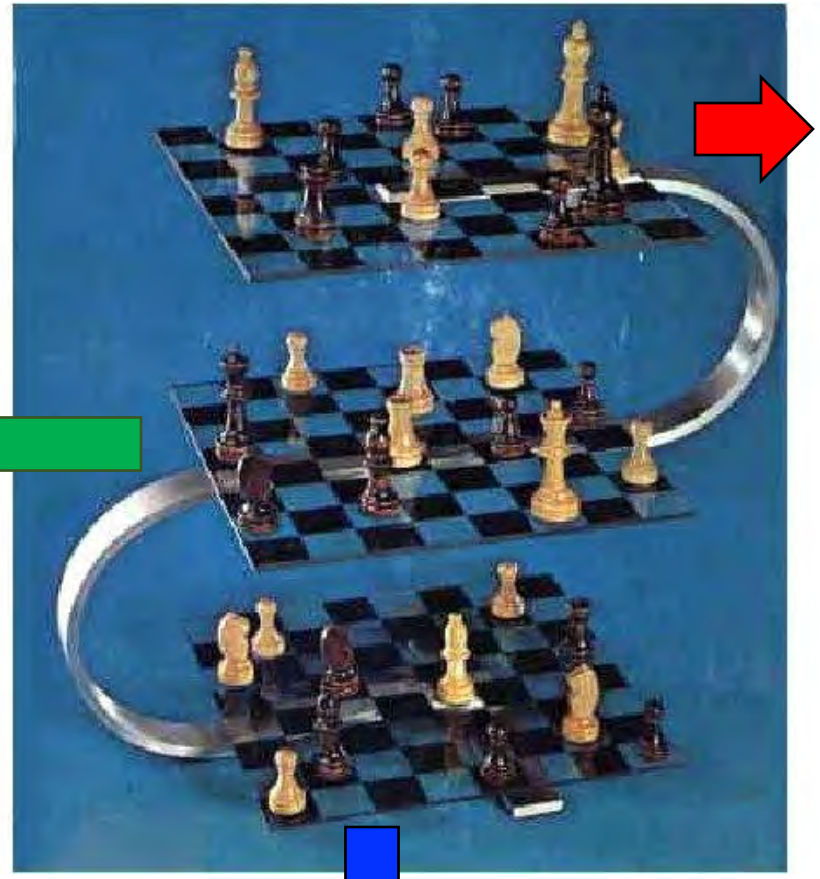
STRATEGIC GAME BOARD

Theradaptive

Biotech Platform

- Sources of sustainable advantage
  - Innovation capability
  - Partnerships and licensees
  - Ethical issues

Differentiation



How to compete

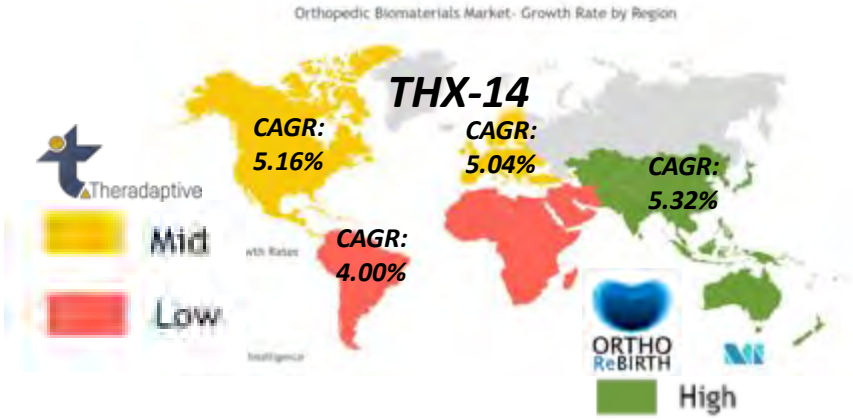
When to compete

- ***Nothing to lose.***
- ***Risk is welcomed.***
- ***Frugality.***

- Enter (New Entrant)
- Invest (Accelerate Approvals)
- Innovate (Portfolio)

e.g.: - AMP 2/THX-14
- Each Protein, a new Patent.

Where to compete



- Product: Recombinant Protein
- Customer(s) and Channels: CMO
- Geographic market(s): Europe and Americas (Clinical Trials)

Entire Regenerative Market

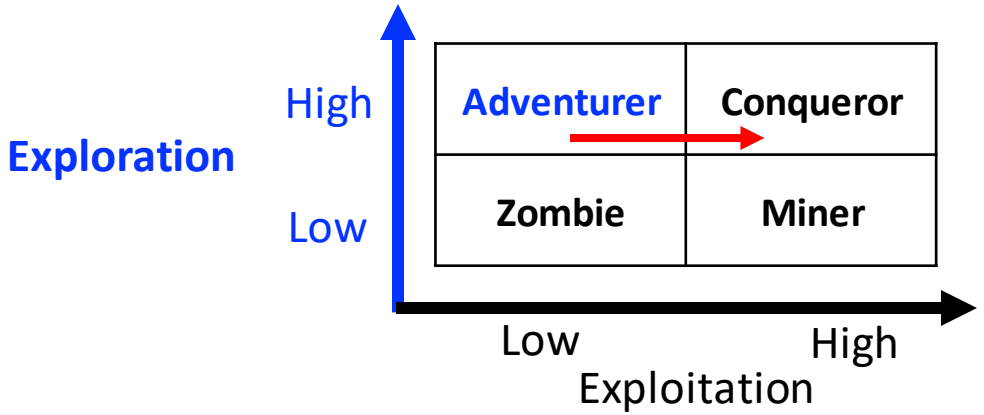
Spine fusion and bone repair

TEMPLATE – STYLE PLANNING

The Vision	- **Future of regenerative medicine.** - **Targeted native tissue repair.** - **Delivering any biologic on any device for any indication.**
The Mission	- **Higher performance and shorter recovery times.** - **Material-binding variants in a paint-like manner .** - **Safer delivery, easier to use, and superior outcome.**
The Values	- **Innovation (choose one product, choose a path)** - **Teamwork** - **Ethic**
The Strategies	- Option to create a separate business for each therapeutic asset **to accelerate liquidity for investors.**

BAD STRATEGY ? (FOUR HALLMARKS)	
Failure to face the challenge	NO
Mistaking goals for strategy	Revenue and Profit?
Bad strategic objectives	NO
Fluff	NO

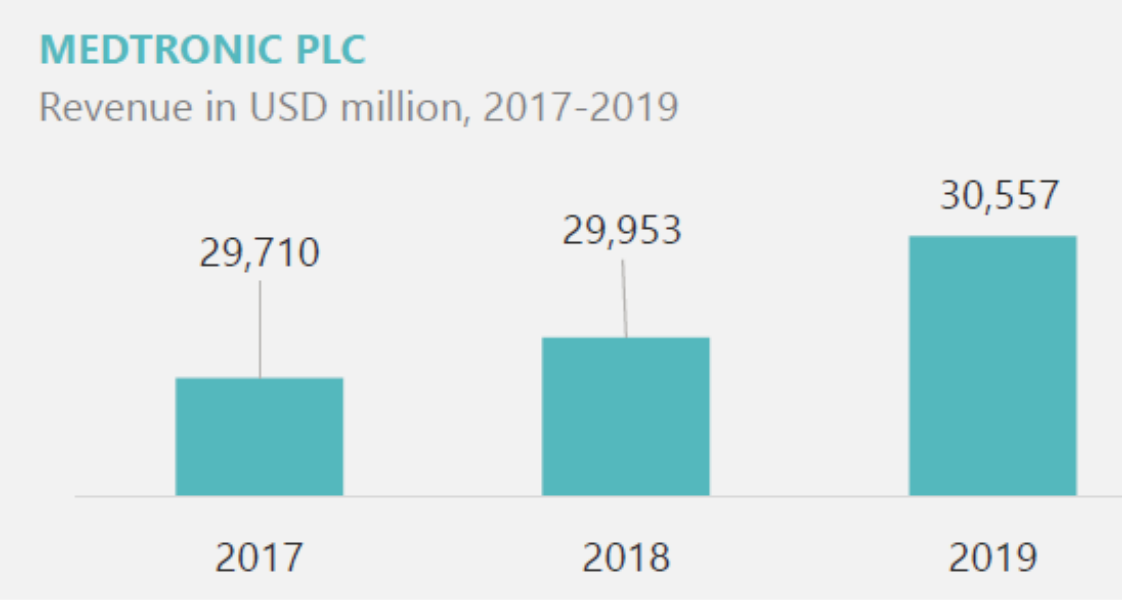
AMBIDEXTROUS?

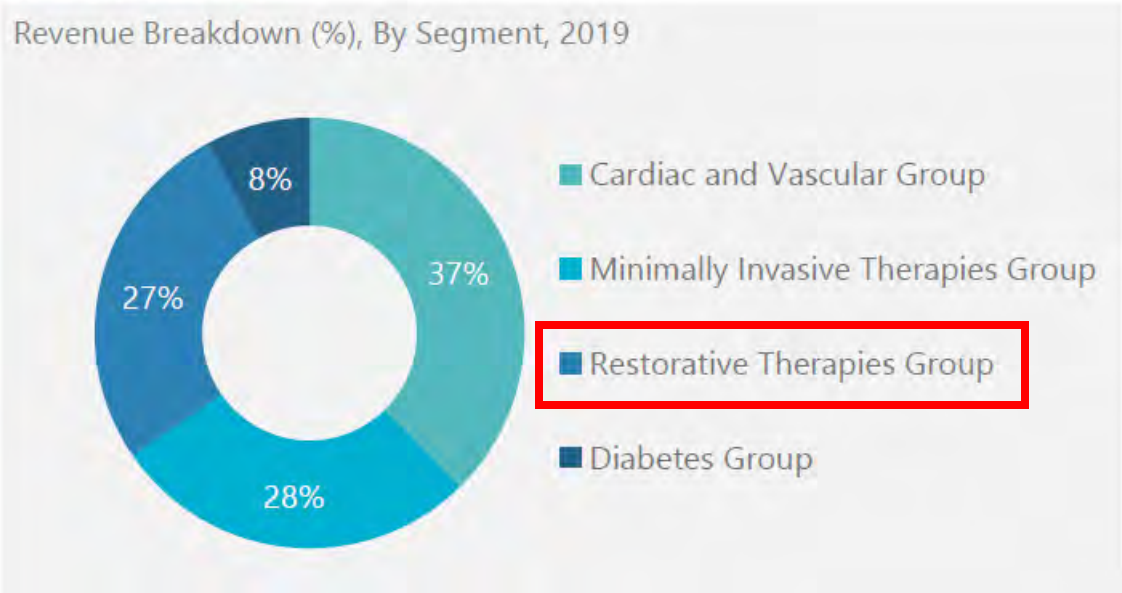


COMPETITIVE ADVANTAGE STRATEGY

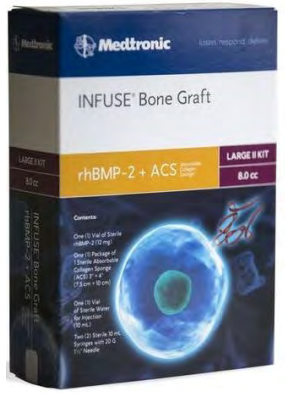
FIVE FORCES	DEFENSES	POSITIONING
RIVALRY	- Product Differentiation - **Price (Shrinking Cost)**	- Innovation and Management
THREAT OF NEW ENTRANTS	- **Investment in human capital, facilities, and machinery** - Improve R&D and manufacturing	- Infrastructure and resources to innovate, produce and delivery timely
BARGAINING POWER OF BUYERS	- Suitable Price - Quality - Delivery - **Marketing Strategy**	- Trustful product - Cost-efficient
BARGAINING POWER OF SUPPLIERS	- Backward integration (licensing)	- Self-sufficiency
THREAT OF SUBSTITUTE PRODUCTS	- Investment in innovation to create new differentiation and defeat price competition.	- Skilled worked force

COMPETITION - MEDTRONIC





- Restorative Therapies Group
  - Revenue 2019 - $8,250M (2019 Revenue)
  - Divisions:
    - $2,970M – Brain 36%
    - $2,640M – Spine 32%
    - $1,320M – Pain 16%
    - $1,320M – Specialty 16%



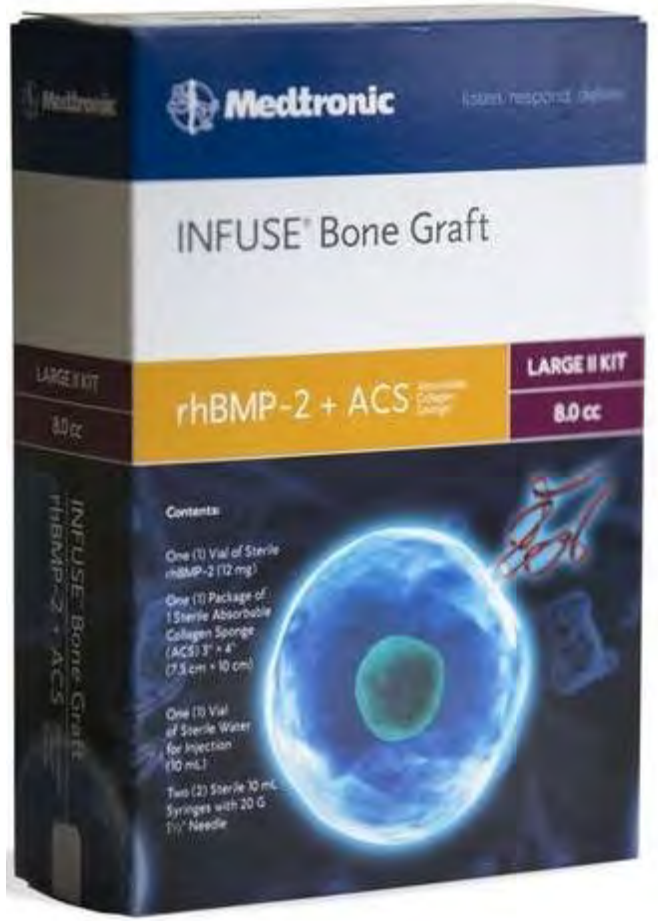
ARTIC-L SPINAL SYSTEM

MAGNIFUSE BONE GRAFT

COMPETITION - MEDTRONIC

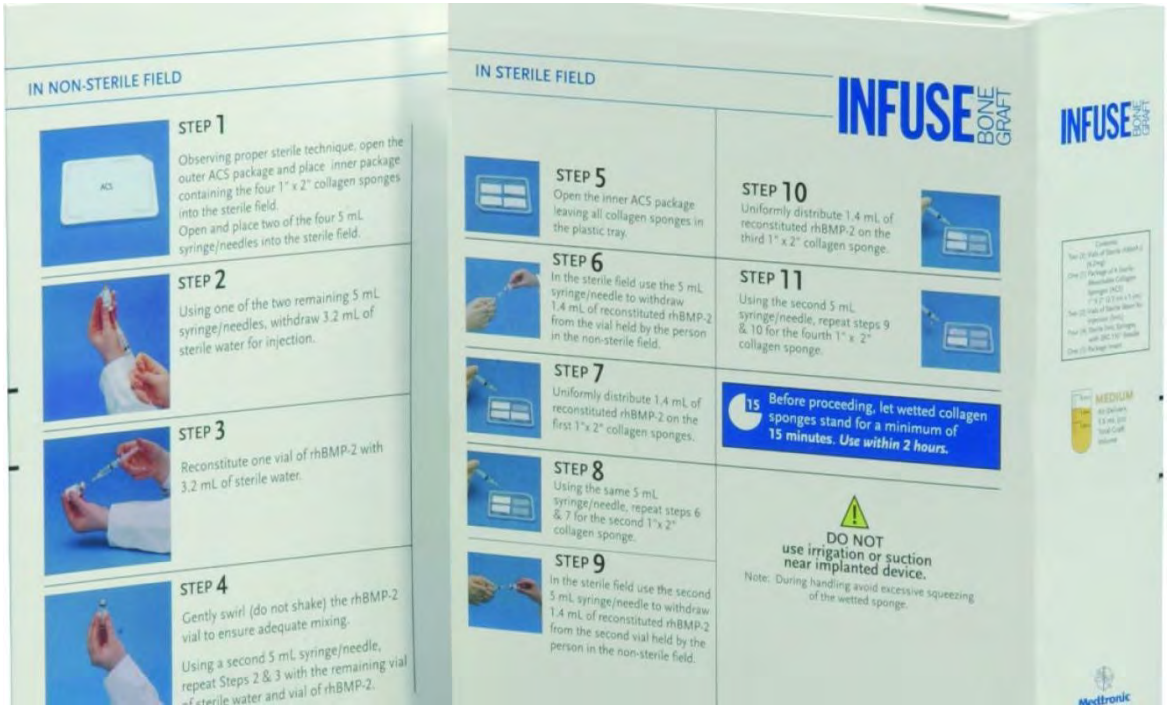
Medtronic - Market leader

- Product: Infuse™ Bone Graft
  - Recombinant Human Bone Morphogenetic Protein (rhBMP-2)
  - Collagen Sponge
- FDA Approval for Spinal Fusion (2002)
- 100,000 spinal fusion procedures / year (2011)
- $750M in sales (2011)
  - $7,500 per package of Infuse



COMPETITION - MEDTRONIC

- Issue with Infuse Bone Graft
  - Localized application
  - Side effects
    - Inflammatory reactions
    - Back and leg pain
    - Radiculitis (pain that spreads through the spinal nerves)
    - Implant displacement
    - Retrograde ejaculation (occurs when semen enters the bladder)
    - Male sterility
    - Cancer
    - Infection
    - Osteolysis (degeneration of bone tissue)
    - Ectopic bone formation (unwanted bone in the spinal canal)
    - Death



COMPETITION - STRYKER

Stryker

- Product: OP-1 Putty
- Uses recombinant human Bone Morphogenetic Protein (BMP-2)
- FDA approval for rare use (2004)
  - Humanitarian exemption
- No FDA approval for spinal fusion (2009)

ETHICS

- Civil Suits
  - Medtronics – Side effect → lawsuits, $460M in settlements
- Criminal Investigations
  - Medtronic paid $40M to settle with the Department of Justice (DOJ)
    - Anti-kickback statute
  - Stryker paid $15M to settle with the DOJ
    - Promoted off-label uses of OP-1 Putty
- Takeaways from Medtronic and Stryker
  - Complete clinical trials
    - Effectiveness
    - Side effects
  - Properly market AMP-2 for regenerative therapies
    - Appropriate patients / Approved indications
  - Origin of bone graft (own body, animals, cadavers, synthetics)

PARTNERING FOR INNOVATION

"At BASF, we don't make a lot of the products you buy.
We make a lot of the products you buy better."

PARTNERING FOR INNOVATION

Theradaptive

AMP-2

+

POTENTIAL PARTNERS AND COMPETITORS

Medtronic

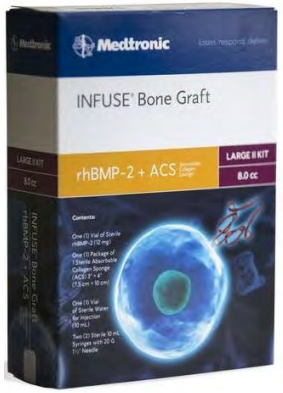
stryker

DePuy Synthes
PART OF THE Johnson & Johnson FAMILY OF COMPANIES

ORTHO ReBIRTH

AlloSource
DOING MORE WITH LIFE

ZIMMER BIOMET



ReBOSSIS

MAGNIFUSE BONE GRAFT

ARTIC-L SPINAL SYSTEM

Future Opportunities

PARTNERING FOR INNOVATION

Theradaptive

AMP-2

+

ORTHO ReBIRTH

ReBOSSIS

THX-14

Regenerative Bone Treatment

AMP-2

+

Medtronic

MAGNIFUSE BONE GRAFT

~~Future~~

~~Substitute~~

Theradaptive

AMP-2

+

ARTIC-L SPINAL SYSTEM

Future Opportunities

R&D FOR INNOVATION

- Process improvements (internal / external)
- New applications for regenerative proteins
- Investigating stem cell technology

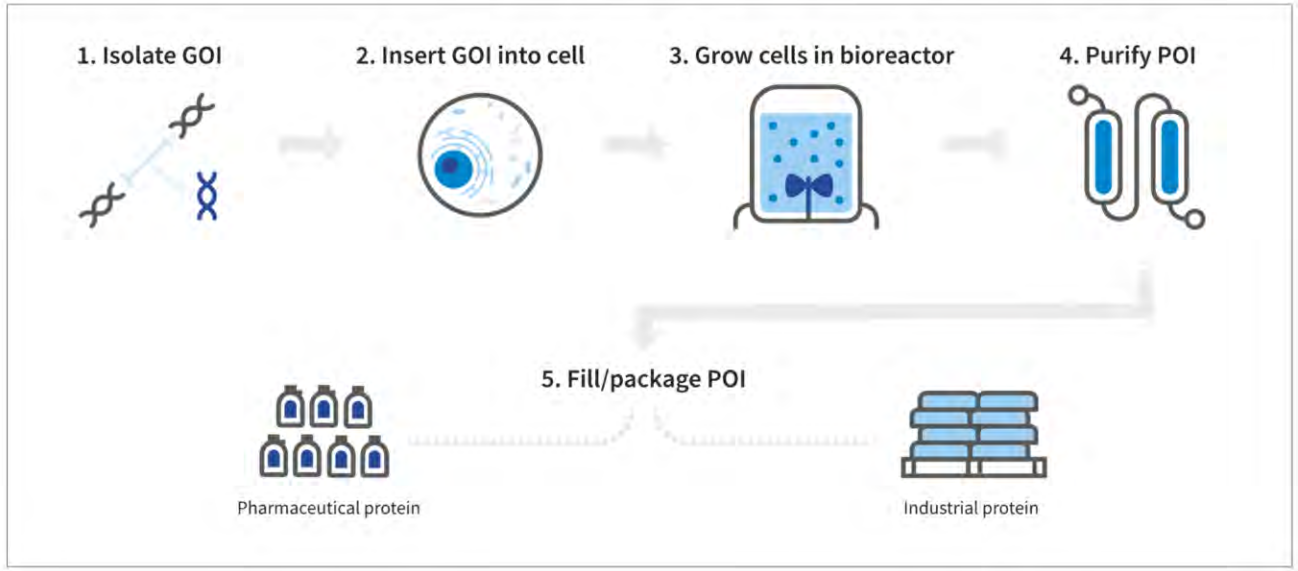
Goals

- Maintain competitive advantage with AMP-2 via process patent
- Expand / diversify product lines

MANUFACTURING / SUPPLY CHAIN

Manufacturing Options

1. Centralized Manufacturing
   - AMP-2 stand-alone paint kits
2. Distributed Manufacturing
   - Future / local 3D printing option
3. Organic or Contract Manufacturing Organizations (CMO)



Supply Chain

1. Current issues:
   - No issues with recombinant protein production
   - Security / IP protection using CMO
2. Future issues:
   - Dependent on manufacturing options
     - Security / IP protection with license partners and CMOs

GOI – Gene of Interest

POI – Protein of Interest

LIFE CYCLE – BEST OWNER

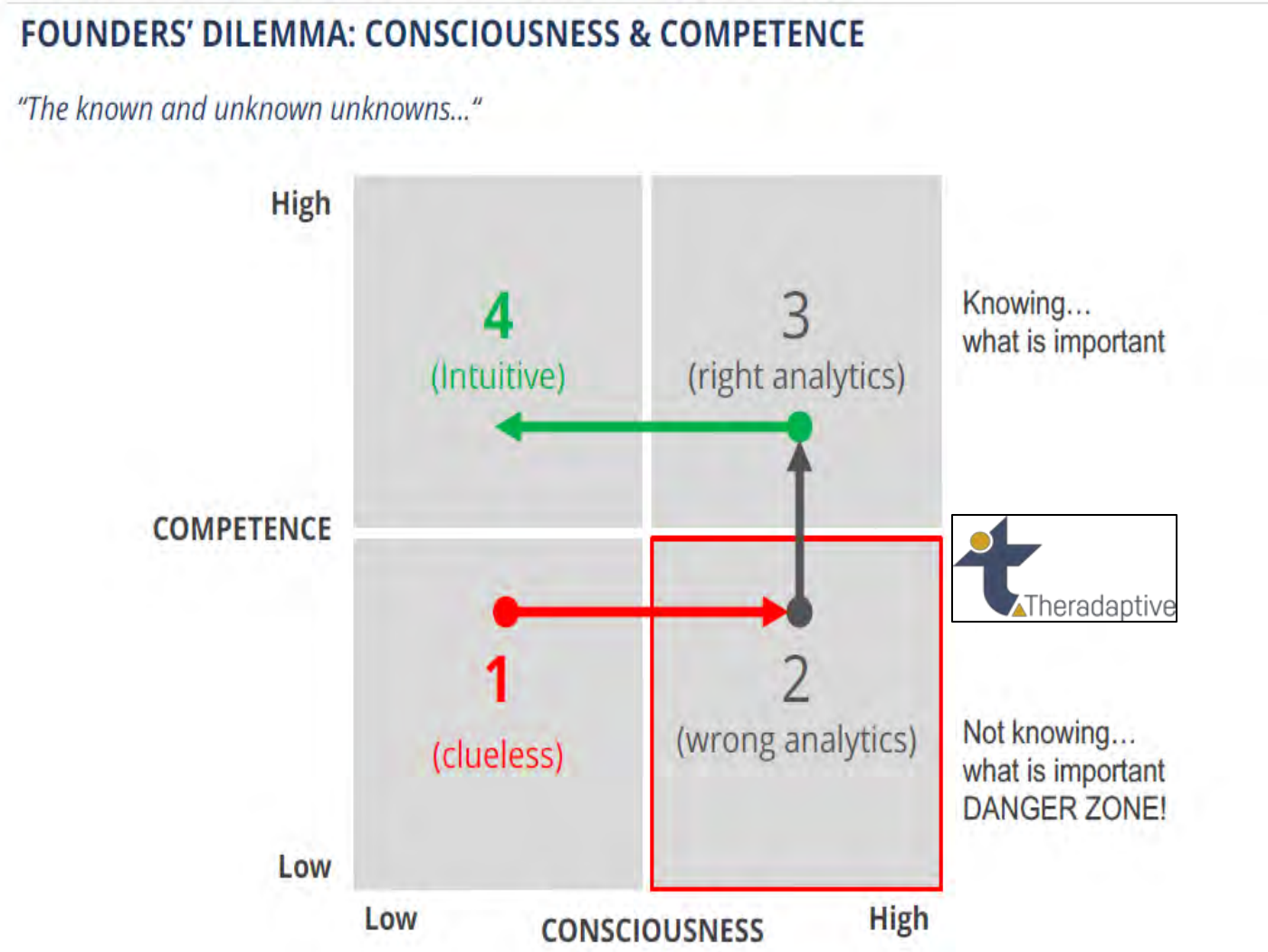
1. The founder came up with the idea for the business.
2. The VC firm provided capital and professional management.
3. Going public provided the early investors a way to realize the value of their work and raised more cash.
4. The large company accelerated the company's growth with a global distribution capability.
5. The private equity firm restructured the company when growth slowed.
6. The last best-owner company applied its skills in success in managing low-growth brands.

CHALLENGES – HUMAN CAPITAL

1. Series A → Series B
   - Business Development
2. R&D → Manufacturing
   - Grow, develop, hire new skill sets
   - Workforce retention
   - Incentivizing diversity to drive innovation

Observation:

- Advisory Board
  - Comprised of MDs and PHDs
  - Need more VCs



Theradaptive

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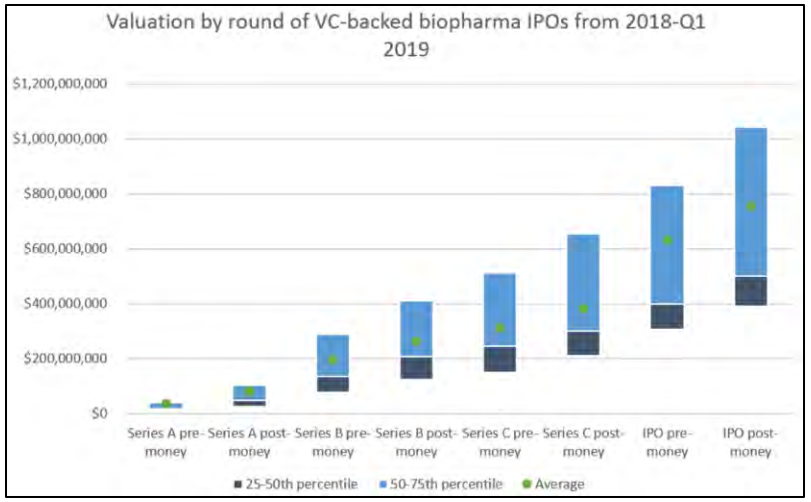
CAPITAL INVESTMENT



ROIC
- Cost of capital
Value

Phase III Endpoint?

Phase II Midpoint

Phase I Midpoint

IDE Filing Prep

Complete Preclinical

2014-2020	2021	2022	2023	2024	2025	2027 ?
$ 10-20 M	***$ 25 M***		***$ 80 M - $250 M***		***$ 500 M - $1B***	
Initial Valuation	*Post Series A Valuation*		*Estimated based on market comps*		*Estimated based on market comps*	

Angel Investments and Contracts = $ 11.2 M

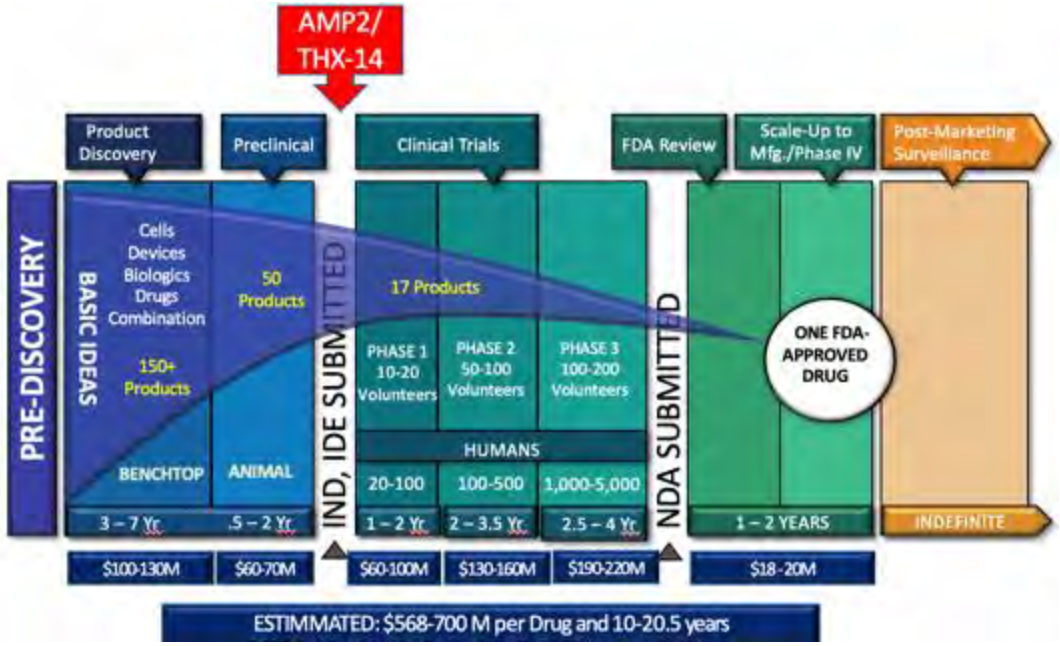
SERIES A = $ 6.2 M

SERIES B PROCESS

SERIES B = $ 20 – 50 M

IDE: Investigational Device Exemption (authorizes start of human trials)

RAISING FUNDS – Is there enough?



JAN 2021 = $17.4 million

1) Angel, DoD, and Veteran Affairs = $11.2 M

2) Series A and Japan-based OrthoRebirth = $ 6.2 M

"This investment will allow us to accelerate our **spinal fusion and trauma programs** into clinical trials in 2022. …. We already have **commitments from investors for our Series B round later in 2021** that will set us up for the next phase of our growth."

https://ryortho.com/breaking/theradaptive-closes-6-2-million-series-a-investment-round/

	200 TRIALS EXPECTED	MINIMUM 50 TRIALS	BMP-2 LOW 50 TRIALS	BMP-2 HIGH 50 TRIALS
• *Year 1 – Filing & 25 patients*	*$770K*	*$770K*	*$1,570K*	*$4,220K*
• *Year 2 – Filing & 75 patients*	*$2,270K*	*$770K*	*$1,570K*	*$4,220K*
• *Year 3 – Filing & 100 patients*	*$3,020K*	*$20K*	*$20K*	*$20K*
• *Year 4-8 Filing*	*$100K*	*$80K*	*$80K*	*$80K*
• *Total Estimate*	≈ *$6,160K*	*$1,640K*	*$3,240K*	*$8,540K*

(6.5 YEARS TO BRING TO THE MARKET -> 2028)

Cost for IDE Filing: $20K /yr RMB-2 L Cost/Surgery: $62K per
Ortho Cost/Surgery: $30K per RMB-2 H Cost/Surgery: $168K per

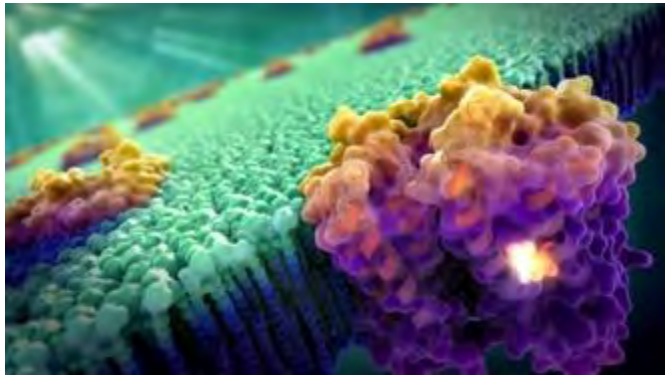
THERADAPTIVE

CONCLUSIONS	RECOMMENDATIONS
1) A platform of biotechnology in regenerative medicine.	1) Market and license based on unique capability.
2) Raise funds for and conduct clinical trials in US, Europe, and South America.	2) Utilize government contacts and contracts to support clinical trials: Wounded Warriors, VA, grants, etc.
3) Spinal fusion and trauma is increasing market with huge competition (Substitute risk). Customized, cheaper and safer products will dominate the market.	3) Pursue dual strategy of improving competition products and direct sales of AMP-2.
4) Multiple production avenues available.	4) Determine manufacturing location to maximize profitability while preserving intellectual property.
5) Recombinant protein is ethically more accepted.	5) Marketing and sales team should highlight this aspect.
6) Maintain non-metabolized formulation for Device Designation and associated reduced trial costs.	6) Lobby and participate in FDA public discussion to maintain definitions.
7) Regenerative orthopedics is driven by cross-market forces and behaviors: injuries and age.	7) Limit negative exposure and liabilities through ethical marketing and sales.

US GOVERNMENT

CONCLUSIONS	RECOMMENDATIONS
1) Device and Drug development and clinical trials are expensive and potentially duplicative internationally.	1a) Expand VA and TriCare coverage of clinical trials. 1b) Develop international equivalency agreements.
2) Biotech development hubs are crucial for success.	2) Support hub development and operations through government policy and funding.
3) US production is desirable for revenue and intellectual property production and protection.	3) Incentivize US production through tax and construction / certification cost reductions and provide venture capital loans and guarentees.
4) Biotech Labor availability is limited.	4) Incentivize STEM education programs and paths.
5) AMP-2 is not likely to be considered for Mobilization or Surge requirements given startup status but will be considered for this scenario.	5a) Incentivize US production through tax and construction / certification cost reductions and provide venture capital loans and guarentees. 5b) Award indefinite delivery indefinite quantity contracts based on either successful R&D completion or clinical trials. 5c) Provide Defense Production Act Title III funds for manufacturing capacity.

QUESTIONS?



ENDNOTES

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