Long Ideas | Healthcare

After Landmark COVID-19 Vaccine Success, Pfizer Looks To The Next Frontier

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Summary

- An interview with Mikael Dolsten, Chief Scientific Officer and President, Worldwide Research, Development and Medical at Pfizer. By Shawn Macomber Seeking Alpha Contributing Editor – Brand Partnerships.
- Pfizer seeks to transfer the success of its "light speed" program to develop a COVID-19 vaccine to several other areas of research.
- Over the next 18 months, the company anticipates potentially delivering a wide-ranging slate of up to ten approvals, and projects up to fifteen pivotal readouts and up to fifteen key proof-of-concept readouts.
- All of this is buoyed by third quarter 2021 revenues of $24.1 billion and a 130% operational growth versus third quarter 2020, which has raised full-year 2021 revenues guidance to a range of $81 to $82 billion.

It may have appeared a miracle from the outside, but the ability of Pfizer to rise to the pandemic occasion and develop a COVID-19 vaccine in record time was no coincidence. It was a result of the 10-year journey Pfizer took to dramatically turnaround its research and development organization. The company, founded in 1849, has been investing in its scientific and technical capabilities for years, helping power a scientific revolution steeped in a strong biology foundation, a modality toolbox with the right depth and breadth, and enhanced decision-making, effectively preparing for a moment none of us saw coming—and met it in spectacular fashion.

For Mikael Dolsten, Pfizer's Chief Scientific Officer and President, Worldwide Research, Development and Medical, it was, after three decades working in the pharmaceutical industry, a profoundly special moment.

"We have built a courageous and decisive culture [at Pfizer]," Dolsten tells Seeking Alpha. "It relies on very strong science technologies integrated from R&D to manufacturing, combining quality, speed, and innovation. And we never let one of them down on behalf of another."

This is no idle boast: Pfizer seems to be beating the general odds in the probability of going from the early stages of studying an investigational vaccine or medicine to full approval by a regulatory agency.

The company has more than tripled its Phase 2 success rate on a five-year rolling average from 2016 to 2020.

Now the mentality of the drive to develop their COVID-19 vaccine—which Pfizer at the time dubbed "Project Lightspeed"—is being applied to several other areas of research.

Could the "impossible" be made possible again?

Pfizer certainly believes so. Over the next eighteen months the company anticipates potentially delivering up to ten approvals, and projects up to fifteen pivotal readouts, and up to fifteen key proof-of-concepts that could potentially ultimately deliver on an exciting next wave of innovation in medicines and vaccines.

If success begets success—and increased revenue funds increased possibility—then recent reported numbers could open new opportunities: On November 2, 2021, the company reported third quarter 2021 revenues of $24.1 billion—which translates to a 130% operational growth versus third quarter 2020—and has raised full-year 2021 revenues guidance to a range of $81 to $82 billion. (Approximately $36 billion of that is expected to come from the approximately 2.3 billion doses of the Pfizer BioNTech COVID-19 vaccine; anticipated to be delivered this fiscal year based on expected ordering patterns through the end of December for the U.S. and through the end of November for the rest of the world.) It's worth remembering, too, as Keith Williams wrote in Seeking Alpha recently, "there has been news from all around the world of increased orders for the Pfizer/BioNTech vaccines including for 2022 and 2023." He further notes, [on] "the African continent, with 17% of the world's population, just 3% of the population has received at least one COVID-19 shot."

But this is not merely about the COVID-19 vaccine. From hospital products to the impressive growth of a host of other treatments in the third quarter of 2021 —e.g., Eliquis up 19% operationally in global revenues; Vyndaqel/Vyndamax up 42% operationally; Inlyta up 30% operationally; Ibrance up 1% operationally; and more—this rising tide is raising far more than one boat.

"I feel very optimistic about the future to come," Dolsten says.

Here are five areas in which we might see the traditional metrics of progress turned on its head once again.

Vaccines

Pfizer is still pushing the envelope across multiple fronts in the COVID-19 vaccine development arena. The company was first to file for and receive an Emergency Use Authorization for the use of a booster for people at highest risk of severe COVID-19, first to receive an Emergency Use Authorization for a COVID-19 vaccine in children 5 through 11 years of age, and recently announced an interim analysis of a clinical trial of its investigational novel COVID-19 oral antiviral —a protease inhibitor— which in high-risk patients demonstrated "89% reduction in risk of COVID-19-related hospitalization or death from any cause compared to placebo in patients treated within three days of symptom onset."

Yet the fight to address unmet medical needs on a global scale with vaccines did not begin, and will not end, with COVID-19.

Pfizer has eight Phase 3 vaccine trials ongoing.

"We are building a deep portfolio around respiratory diseases," Dolsten says, pointing to the recent approval of Prevnar 20 in adults 18 and older, which he calls, "by far the most comprehensive coverage of pneumococcal strains causing pneumonia or invasive disease." Next year, he adds, the company expects to have a readout for the infant version of Prevnar 20, as well as data from an ongoing study examining a potential co-administration of Prevnar 20 in adults and the COVID-19 vaccine.

Looking forward, Phase III studies of a vaccine for respiratory syncytial virus (RSV), Dolsten says, have begun after seeing "very promising efficacy" in a Phase II study in a small number of participants. "We are excited because RSV...is one of the major burdens of disease without prevention and very limited treatment options in both newborn infants and adults." The Pfizer bivalent RSVpreF vaccine candidate targets both the RSV A and RSV B subtypes. It is now in Phase 3 testing for two potential indications – immunization of pregnant women to protect their infants and immunization of older adults to reduce their burden of RSV disease.

Again, the speed here is unprecedented.

Further, the "capabilities and the capacity" derived from Pfizer's COVID-19 experience are being re-channeled toward other vaccine development programs.

Oncology

Oncology, Pfizer's largest R&D area, is focused on four areas—breast cancer, prostate cancer, precision medicine, and hematology.

In the breast cancer arena, the company's Ibrance is the market leading CDK 4/6 inhibitor for postmenopausal women or in men with HR+, HER2-metastatic breast cancer. The company is also building on its pioneering legacy in breast cancer with three next-generation CDK inhibitors (CDK 2/4/6; CDK2-selective; CKD4-selective) that seek to expand CDK inhibition as backbone therapy in HR+ disease. And in July, Pfizer announced a global collaboration with Arvinas to develop and commercialize ARV-471, a promising oral PROTAC that is understood to have the potential to degrade and block estrogen receptors in hormonally driven breast cancers. "We see that as a unique opportunity, both in the cell cycle and the hormone dependency pathway, to bring innovation and new horizons into early to late-stage breast cancer treatment, and combination potential with Ibrance and our next generation CDK portfolio," Dolsten says.

There is also the potential for progress in prostate cancer with the TALAPRO-2 trial, which is investigating the combination of Pfizer's PARP inhibitor talazoparib with the androgen receptor inhibitor enzalutamide. If positive, this new combination approach offers the potential for better treatment outcomes for men suffering from castration-resistant prostate cancer.

Meanwhile, the fight against blood cancer heats up with elranatamab, the company's investigational B-cell maturation antigen (BCMA) CD3-targeted bispecific antibody that has the potential to improve outcomes in multiple myeloma and is currently in a registrational trial for triple refractory patients suffering from that disease. This advance in the company's hematology portfolio is bolstered by the recent acquisition of Trillium, a biotech company that has novel immuno-oncology checkpoint inhibitors TTI-622 and -621 which block the signal-regulatory protein α (SIRPα)–CD47 axis.

"We see an opportunity to expand our blood cancer franchise," Dolsten says, "we plan to accelerate the development of SIRPα fusion proteins as the next potential immune checkpoint backbone and explore combinations within our own portfolio, including a potential combination with elranatamab in multiple myeloma." The company's recent business development deals in oncology strengthen its innovative pipeline, in much the same way that, say, the acquisition of Array Biopharmaceuticals in 2019 served as a force multiplier in its efforts to increase the number of "high-potential targeted investigational cancer therapies" in its pipeline—including BRAF-mutant metastatic colorectal cancer, melanoma, and more.

"We believe in being first-in-class and first in technology," Dolsten says. "And to make huge impact, it's all built upon combination strategies that evolve over time."

Rare disease

This growing area for Pfizer, expanded substantially last year with the launch of Vyndaqel / Vyndamax (tafamidis), an agent designed to combat TTR amyloidosis cardiomyopathy, and novel technology focused on gene therapy balanced with other drug design modalities.

This highlights Pfizer's "courage," too, investing in new modalities that have the potential to transform outcomes ahead of the competition.

The company's pipeline of twelve investigational gene therapy candidates in pre-clinical and clinical development is now targeting hemophilia B, hemophilia A, and Duchenne's muscular dystrophy— but it's just the beginning, according to Dolsten. "Pfizer has one of the most—if not *the* most—comprehensive gene therapy platforms in the industry," he says. "The dramatic effect of gene therapy is that a single infusion may lead to a potentially transformative outcome."

Again, it's been built by internal investment, acquisitions, and partnerships with companies such as Sangamo Therapeutics, Bamboo, and Spark Therapeutics.

When Pfizer's gene therapies converge with its mRNA platform, the leaps forward could be even greater.

"We have started now to build plans to explore gene editing at large scale," Dolsten says, "which means that you are not providing an extra correct gene like you do with gene therapy, but you're actually rewriting the DNA code in the human cells to correct a faulty order of the DNA-based parents."

The future truly is now.

Internal Medicine

In this area, Pfizer is striving to address improved ways to treat intractable chronic illnesses by better targeting the underlying drivers of those diseases.

For example, Pfizer's investigational oral GLP-1 molecule builds upon studies showing that injectable GLP-1s powerfully treat diabetes and obesity, and also potentially NASH (Non-Alcoholic Steatohepatitis, which can lead to liver failure and death), while simultaneously allowing for more advantageous oral administration.

"We are very pleased to work towards addressing some of these very large burdens on society," Dolsten says, "that affect people, that affect social life, that affect the economy of the world."

Immunology and Inflammation

Here Pfizer has pioneered how to address cytokine pathways with its JAK inhibitors. Xeljanz was the first approved JAK inhibitor for rheumatoid arthritis and certain other inflammatory and auto-immune conditions. Recently proposed updates to the FDA's safety labelling for the class potentially open the door for the company to win approvals for a new wave of JAK inhibitors.

Additionally, Pfizer's pipeline includes other oral and topical kinase inhibitors for diseases such as atopic dermatitis, inflammatory bowel disease, alopecia, vitiligo – an auto-immune disease that causes depigmentation of the skin, along with other inflammatory disorders.

Beyond the oral JAK portfolio, Pfizer is diversifying in Immunology and Inflammation with potential therapies that work to modulate immune responses with several potentially first-or-best-in-class targets such as TL1a in ulcerative colitis, IFN-beta in dermatomyositis, and a topical, high-potency PDE4+ in atopic dermatitis.

In Closing

The key, again, is how the breadth of Pfizer's work continues to pay synergistic dividends.

"The way we analyze data represents a platform for all our therapeutic areas that allows us to very rapidly move an insight into a technology or a disease from one area to another," Dolsten says. "We have particularly been thrilled to see that so many diseases have underlying immunological abnormalities, creating bridges between medicines from oncology to immunology to metabolic disease. So, I think there is a clear vision in how our R&D engine uses all of its cylinders, the science in each of the research units."

It's all evidence, Dolsten says, that we are in a technological and scientific renaissance.

"On the technology side, it's just extraordinary that we have been able to bring together such powerful ways to design drugs and vaccines demonstrated by the mRNA platform," he says. "In biology we now are able to bring together large pre-clinical and human clinical datasets that give us completely unprecedented insights into the cells and the pathways that drive disease in humans and why certain patients may have different risk factors than others. That can allow us to drive both precision medicine and sometimes address disease nodes that are more common across many patients. It is a unique time with science and technology and computational biomedicine all converging."

As the last two years have clearly demonstrated, you never know when that convergence will become a matter of global life or death.

If luck is "when preparation meets opportunity," as the Roman philosopher Seneca said, then Pfizer is one of the luckiest companies to ever exist – for the good of its investors and the benefit of patients.

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