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How Will Pfizer Leverage External Innovation After BioNTech Jackpot?

by Lucie Ellis-Taitt

Uwe Schoenbeck, CSO of external science and innovation at Pfizer, knows the company set itself a high bar during the COVID-19 pandemic after rapidly bringing a breakthrough vaccine to market. While the circumstances for the development of Comirnaty were truly unique, Pfizer does not expect to rest on its laurels when it comes to innovative R&D.

The past two years have been transformational for *Pfizer Inc.*, thanks to its partnership with German biotech firm *BioNTech SE*. Uwe Schoenbeck, senior vice president and chief scientific officer, external science and innovation at Pfizer, spoke to *In Vivo* about how external innovation and internal agility are key to the company's future success.

Heading into 2022, Pfizer – now a household name the world over thanks to the success of its COVID-19 vaccine in partnership with BioNTech – is focused on "staying on the cutting edge of science." The company is "identifying strong partners in the academic world and in the biotech world, that are able to help us and work with us on making the changes we need for patients in the gene therapy, mRNA and in degrader spaces," Schoenbeck noted.

To maintain the momentum it has created through the COVID-19 pandemic, Pfizer will draw on its wide portfolio of novel modalities and its ability to select the best partners in revolutionary R&D, the executive said.

But in a recent talk at the October HLTH conference,
CEO Albert Bourla admitted that Pfizer had some way to go to convince market spectators that its mRNA COVID vaccine with BioNTech was not a one-off success story, in terms of bringing a novel modality to market and seeing success quickly. An issue that has plagued the first movers in gene therapy is that while the treatments work, the financial gains have not matched expectations.

UWE SCHOENBECK *Source: Pfizer*

Even if there remains skepticism about the sustainability and success of Pfizer's novel pipeline, which includes gene therapies, mRNA drugs and novel protein degrader therapeutics, Bourla said Pfizer had been able to prove during the pandemic that a big pharma company could move with the speed of a biotech. "The biggest thing is the culture inside the company ... we have shown to the entire company that nothing is impossible," he said. Now branded Comirnaty (a mashup of community, immunity, mRNA and COVID), Pfizer first teamed up with BioNTech to develop the COVID-19 vaccine BNT162b2 in March 2020. By November 2020, Phase III trials were complete and before the end of that year, Pfizer and BioNTech became the first companies anywhere in the world to get approval for a COVID-19 vaccination (*see Exhibit 1*). On 2 December, the Medicines & Healthcare Products Regulatory Agency (MHRA) in the UK granted a temporary authorization for emergency use for Comirnaty against COVID-19.

Exhibit 1.

Date	Event
17 March 2020	Pfizer and BioNTech agree to a letter of intent regarding the co-development and distribution (excluding China) of a potential mRNA-based vaccine aimed at preventing COVID-19 infection
5 May 2020	First participants receive vaccine doses in the US as part of global COVID-19 mRNA vaccine development program
13 July 2020	Pfizer and BioNTech get FDA Fast Track Designation for two investigational mRNA-based vaccine candidates against SARS-CoV-2
28 July 2020	The pair choose a lead mRNA vaccine candidate against COVID-19 and commence a

	pivotal Phase II/III global study
6 October 2020	Rolling submission initiated with European Medicines Agency for SARS-CoV-2 vaccine candidate BNT162b2
18 November 2020	Pfizer and BioNTech conclude Phase III study of BNT162b2, meeting all primary efficacy endpoints
2 December 2020	BNT162b2 is the first COVID-19 vaccine to receive emergency use approval, eith the UK's MHRA granting a temporary authorization
11 December 2020	The vaccine secures emergency use authorization in the US; followed by approval in Europe in late December
23 August 2021	Comirnaty becomes the first COVID-19 vaccine to be granted FDA approval; more than 1.2 billion Pfizer-BioNTech vaccine doses have been delivered to more than 120 countries or territories around the world since December 2020

Source: Drugs.Com; Press Releases; Scrip

Pfizer sees its COVID-19 vaccine as a "lightspeed" project. The speed and agility shown in the development of Comirnaty are approaches Pfizer wants to replicate elsewhere. "Everyone [at Pfizer] now, in addition to vaccines, they want to have their lightspeed moment, on colon cancer, rare diseases, internal medicine, or neuroinflammation, and they are all bringing projects that they want to run with the same speed and the same ambition," Bourla said during the HLTH presentation.

Pfizer's R&D is focused on five key therapeutic areas: vaccines, oncology, rare disease, internal medicine and inflammation and immunology.

Seeking Innovation

Innovation must have meaningful application, said Schoenbeck. "Innovation is novel approaches that have the potential for true breakthroughs for patients," he defined. When assessing projects to bring into the fold, Schoenbeck asks, "Is it just interesting biology or an interesting technology, or does it really have all it takes to translate into a breakthrough therapy down the road?"

"That's the kind of innovation that we're really trying to focus in on, the kind we are trying to

enable through partnerships, and then try to really leverage to bring to fruition," he said. As an example, he highlighted mRNA as one modality for the Pfizer pipeline that fits the bill for true innovation, but he added, "We also have really game-changing activities in the gene therapy space and other areas as well."

For external innovation to work, classical business development teams, corporate venture capital functions and Pfizer's centers for therapeutic innovation (CTI) group, as well wet bench-based functions, must all work together under one umbrella, Schoenbeck emphasized. "Transparency is the key," he said. "In this kind of role, you need to internally integrate a lot of different functions. But you also have to externally manage the interactions." Working with external partners, "we have to make sure that internally, everything is lining up properly, to give the project the best chance."

He added: "The bottom line really is that you're going to have to be very transparent in your communication. You have to be very frank in the expectations. And you have to be very open minded, to really be able to address all the different approaches that are out there that you want to work in."

Appetite For Risk

After the success of the COVID-19 vaccine, the bar has been raised for what Pfizer will produce next.

Schoenbeck noted that COVID-19 was a very unique situation, and he praised the work of many pharma companies, biotechs and government agencies that were able to work together in new ways. "It was a demonstration of what can be done in the health care sector," he said. "We have around 280 different components in our vaccine, we have close to 90 different providers and more than 19 different countries to work with. The supply chain must be established to make sure everything is working. We have seen what can be done and what can be accelerated. This won't work for every program, obviously, but hopefully we can bring some of this innovation from the product development efforts into other projects."

"We are hopeful that we will carry over some of these lessons as we go into the next level, not just on mRNA vaccines and in areas like flu and other infectious disease vaccines, but also other developments," including gene therapies and more established modalities. Schoenbeck does not want to see companies cutting corners, but he also does not want developers to get dragged back to the slower, historic approach "when we have seen what can be optimized."

Pfizer is continuing to invest in and expand its leadership in the mRNA space, both in vaccines and in RNA therapeutic approaches. The company is also investing heavily into its gene therapy portfolio. "We have seen innovative shifts in the overall portfolio of Pfizer. Now we're really looking for truly differentiated novel approaches," Schoenbeck said.

What does this mean for the big pharma's appetite for risk? True novelty means success is harder to predict.

"If you do truly differentiated mechanisms, they have a little bit more of an inherent risk than if you're trying to give me-toos and me-betters," Schoenbeck noted. In parallel to shifting its pipeline focus towards novel modalities, Pfizer has also "revamped" how it advances preclinical and clinical pipeline programs. "Historically, Pfizer has not necessarily been a leader when it comes to rates of progression times in the portfolio. However, over the last three to five years, we've really had a turnaround in R&D by applying a number of steps, including just more rigor in the early stages." He noted that Pfizer has more recently become a leader when it comes to success rates and cycle times.

Looking at the company's pipeline over time, data from Pharmaprojects shows that Pfizer has significantly reduced the number of early-stage programs it runs, with the size of its in-house preclinical pipeline shirking over time, in line with its efforts to streamline and work more with external partners (*see Exhibit 2*).

Exhibit 2.

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"As we have seen, sometimes you have to take risks of the unknown mRNA vaccines. You have to take a leap of faith, but this was based on what we felt we saw in the partnership with BioNTech. With the data we had available, we really felt it was the right fit. And as it turned out, it was the right strategy to go after," Schoenbeck said.

As a result, he thinks Pfizer has built up more confidence, and that even with several novel modalities at play, like gene therapy and RNA, "we are in a good position to make sure we can deliver the portfolio, despite the higher risks of innovative projects."

Constructing Successful Partnerships

The way in which larger biopharma companies interact with biotech and smaller pharma partners had evolved over recent years, Schoenbeck noted. Thinking back to when he started out in pharma, the "approach in general was more, we give you the funding, you give us the IP and the assets, and then we parted ways." But he said this approach was not very successful. Over the

past few years, big pharma – Pfizer included – has changed. Schoenbeck said Pfizer was able to offer a wider range of investment vehicles to meet the needs of its partners. "We have done research collaborations, licensing option deals, acquisitions, seed investments, equity investments, and so on and so forth. The range of investment vehicles has become much broader," he said. "We really want to make sure that you bring the best for both parties to the table. And together do something that neither of us can do alone. That is the key motivation behind partnering for us."

As an example, Schoenbeck noted Pfizer's 2014 partnership with gene therapy company Spark Therapeutics, for the development of PF-6838435 (fidanacogene elaparvovec) for hemophilia B.

While Pfizer had limited experience in this area, Spark "had some true clinical expertise affiliated with them," Schoenbeck said. Spark continued to run Phase I and II studies for the gene therapy asset, before Pfizer took on responsibility for Phase III. "We really have worked with the investigators, making sure to bring the best knowledge, the best expertise and the best capabilities into the partnership."

PF-6838435 is a novel, investigational vector that contains a bio-engineered adeno-associated virus capsid (protein shell) and a high-activity human coagulation factor IX gene. It is hoped that, once treated, hemophilia B patients will be able to produce factor IX themselves, rather than having to regularly inject factor IX. The treatment has shown impressive efficacy data with an annualized bleed rate below one. Phase III data for PF-6838435 from the BENEGENE-2 trial are expected in the first quarter of 2023. Spark Therapeutics was acquired by *Roche Holding AG* in 2019, in a deal valued at $4.8bn. (Also see "*Roche $4.8bn Buy Sparks Hemophilia Gene Therapy Race* " - Scrip, 25 Feb, 2019.)

"Strong partnerships are the key to success," Schoenbeck told *In Vivo*. He noted that more recently, companies had been coming together to focus on particular disease areas or development programs, which was not usual of big pharma in the past. In the oncology space, Schoenbeck noted as an example, combination therapy was a key driver. "Any one company can only run so many Phase II and III studies in their portfolio. If you want to maximize the opportunity for patients from your drugs, you really have to test them in a number of combinations."

He expects this approach to take hold outside of oncology as well, in areas like autoimmune and cardiovascular disease. "We'll see more cases where large pharma companies will get together and partner."

Positive View For 2022

While Comirnaty sales will continue to boost Pfizer in 2022, market experts will also be waiting to see how the company lives up to the successes it saw in 2021. Building its longer-term

pipeline still holds a high degree of risk due to its emphasis on novel approaches like gene therapy. Bank of America has described the big pharma as "transitioning to innovative biopharma," while JP Morgan analysts have called its pipeline "a work in progress."

Overall, though, the horizon is bright for Pfizer in 2022, particularly for vaccine sales. JP Morgan analysts, in a 3 November note, said Pfizer's preliminary $29bn 2022 outlook for Comirnaty was "conservative." The company will be able to expand the vaccine's reach even further in 2022, through additional booster and adolescent vaccination programs – adding more fuel to its R&D pipeline and its ability to seek competitive partnerships.