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Flight Of The Navigator: Bluebird bio's Andrew Obenshain

The gene therapy firm is transitioning to a commercial organization

by Jo Shorthouse

For 12 years, bluebird bio has been developing gene therapies for rare genetic disease and now, with two approvals under its belt, the company is continuing to explore uncharted territory as it brings forward innovative new treatments. Holding the map is CEO Andrew Obenshain.

When deciding on its company moniker in 2010, *bluebird bio* said the name exemplified its intent to set a bold new course for the future. The Eastern Bluebird is known to be a symbol of transition and renewal as well as a competitive and disciplined bird, it said at the time, traits that were reflected in the company's passion for transforming the lives of patients and their families.

Twelve years down the line and two therapy approvals later, the company continues to set its stall by the characteristics of transition and renewal. The last two years have been punctuated by an evolution of what the company looks like, develops, and how it works with major stakeholders. The organization has changed shape by spinning out its oncology arm, restructuring to extend its cash runway, exiting commercial activities in Europe after failing to secure reimbursement for gene therapy Zynteglo (betibeglogene autotemcel), and debuting an innovative outcomes-based contracting strategy in the US.

The other major change has been a new leader, Andrew Obenshain, who became CEO in January 2021 when predecessor Nick Leschly became CEO of the company's oncology spinoff. Not that Obenshain is a new bird in the nest, he has worked with the company since 2016 as head of Europe, and then as president of its Severe Genetic Diseases division. Having previously worked for *Shire Pharmaceuticals Group PLC* as general manager for France and Benelux, responsible for a portfolio that included seven rare disease products, and prior to that for *Sanofi Genzyme*,

Obenshain has spent his career working alongside researchers, developers, regulators, and payers have pushed forward new strategies for cell and gene therapy.

His career path took him further, to becoming the leader of a pioneering company during yet another transition, this time at a fully commercial company. 2023 is set to be a huge year for bluebird, with two newly approved therapies to commercialize and a third on the horizon.

Following the August 2022 FDA approval of Zynteglo for the treatment of children and adults with beta-thalassemia who require regular red blood cell transfusions, the company is progressing through launch plans and is on track for first apheresis (cell collection). It has also completed the activation of its first wave of qualified treatment centers, expecting to scale these to 40 to 50 by the end of 2023. At the time of writing, the company had signed outcomes-based agreements with pharmacy benefit managers (PBMs) representing more than 40 national and regional plans.

The company will not see revenue from Zynteglo until it is infused into patients, which will take months due to the *ex vivo* gene therapy's complex manufacturing and quality control process. The list price for Zynteglo is $2.8m, with an 80% payback option for patients who do not achieve and maintain transfusion independence in the two years following treatment. The investment bank Raymond James estimates that peak sales of the gene therapy should reach around $206m in 2027. (Also see "*Bluebird's Zynteglo Launch Under Way, But First Revenue Will Take Months*" - Scrip, 18 Aug, 2022.)

In September 2022, the FDA granted accelerated approval for Skysona (elivaldogene autotemcel) to slow the progression of neurologic dysfunction in boys 4 to 17 years of age with early, active cerebral adrenoleukodystrophy (CALD). Three QTCs have been activated for this therapy, and the company anticipates commercial readiness for Skysona, with a list price of $3m, by the end of 2022. Unlike Zynteglo, Skysona is not subject to a outcomes-based payment scheme.

Bluebird plans to submit the sickle cell gene therapy lovotibeglogene autotemcel (lovo-cel) to the FDA in the first quarter of 2023 and could potentially be launched by the end of the year. Could bluebird be looking at three commercialized products by the end of 2023? "I'll leave that to the FDA," Obenshain diplomatically tells *In Vivo*.

Whether 2023 brings two successfully launched therapies, or three, the grooves made by commercialization of Zynteglo and Skysona will ultimately benefit the launch of lovo-cel. It will be the same physicians using Zynteglo that will be using lovo-cel at the same transplant centers.

Obenshain is especially excited about the potential for lovo-cel's use in the US Black community, which has been "significantly underserved" and "under invested in". He said: "The potential to bring a solution to this patient community is incredibly gratifying."

Ruffling Feathers

Bold commercial decisions taken by Obenshain, and the wider bluebird team have led to this point of transition, taking the company from nest builder to fully fledged trailblazer. But those decisions have not been taken without a huge amount of consideration. “I’m a big believer that you don’t make decisions in a silo, you make them with your team,” Obenshain said. “I believe in sweating the details of the decision because it's the decision that matters. You can't always control the outcome, even if you make a good decision.”

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The company has two principles that it follows universally for making those big decisions: taking the long-term view and keeping focus on its mission. Obenshain and his team consider not just what is best for bluebird and the patients that it serves, but also for the whole gene therapy industry. While these types of commercial decisions are never easy, he says, these two principles help to clarify and points the organization toward its “true north.”

Having now brought forward two of the five approved therapies in the US, those decisions have come to bear in a positive way, both for the company, and for the gene therapy industry. Some strategic choices are easier to make than others; bluebird’s innovative outcomes-based contracting strategy with payers for Zynteglo was made based on insights from the payers themselves. (Also see "*Zynteglo Could Be Gene Therapy Test Case For Viability Of Outcomes-Based Contracts – UHC Exec*" - Pink Sheet, 21 Jun, 2022.)

With Zynteglo, bluebird has a therapy with a high efficacy rate but a small risk of failure in its clinical data (in clinical studies 89% of patients achieved transfusion independence). However, having an endpoint that was easily measurable – transfusion independence – made the reimbursement strategy simpler, explained Obenshain. “What we learned from the payers, which actually surprised us a little bit, is they don't want to look for more than a year or two out, they want something they can measure quickly and easily, and they want to mitigate the risks,” he said.

Rationalization aside, some decisions cut deeper than others. “The decision to leave Europe was heartbreaking,” said Obenshain when discussing bluebird’s 2021 exit from the continent to prioritize the US market when European payers did not recognize the value in the $3m therapy.

As a child Obenshain lived in London, before moving to Belgium, then France, and finally Switzerland before moving to the US. Despite the American accent his cultural identity hangs somewhere over the Atlantic, he explains. (Also see "*Bluebird Exits Europe, Casting Clouds Over Gene Therapy Commercial Effort*" - Scrip, 9 Aug, 2021.)

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Despite bluebird's commitment to clinical sites, patient communities, regulators, and even governments and payers at first, there "really wasn't a decision," the CEO said. "There was only one path forward that we could have taken. So as much as we sweated, I really think that there was no other option to us. Looking on that today, the fact that we're around as a company and able to bring these therapies forward, at the very least in one geography, it owes in large part to the fact that we made those really difficult decisions then."

The value of Zynteglo has been recognized in the US, with an ICER report validating that the cost is justified up to $3m. (Also see "*Zynteglo Is Cost Effective At $2.1M, ICER Proposes; Validation For Bluebird's Pivot To US?*" - Pink Sheet, 15 Apr, 2022.)

Bluebird is fully focused on the US, said Obenshain, to show that it can commercially scale the therapy, and take some risk and uncertainty out of the system for payers. The hope is that this, in turn, will help the gene therapy industry—and maybe, someday, bluebird -- move forward not just in one country, but many markets.

A Hard 12 Months

The organization has had a particularly hard 12 months of decision making. In April, it had to lay off 30% of its workforce and deprioritize some investments to free up capital for upcoming launches, aiming to deliver up to $160m in cost savings over the next two years. (Also see "*Bluebird Bio Restructures Amid Financial Woes, But Will It Fly?*" - Scrip, 5 Apr, 2022.)

Two years of taking tough decisions mean that the firm is now ahead of the curve, said Obenshain, and prepared for the macroeconomic headwinds that have been battering the biopharma industry since February 2022 when the biotech bubble burst and valuations floored.

Remember that the Eastern Bluebird is a competitive and disciplined creature? That still stands to this day, he said. The company has it's spend under control, it is operationally sound, and has hit all its milestones this year, said Obenshain. It is also producing therapies that offer clinical

value. “That amalgamation of an internal company that can really make hard decisions and has discipline, combined with therapies that bring value to the healthcare system, means that we're in a good position to get through this tough time,” he opined.

The tough times over the last year have been eclipsed by the first approvals in the company’s 12-year history, and Obenshain’s reaction to these events is visceral. He described the emotion when Zynteglo got approved, “I thought it’d be difficult to top that, then Syksona got approved,” he recalls.

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Having been involved in the biotech industry for over 20 years, the weight of bluebird’s accomplishments to date are not lost on him. Its place in the history of medicine has now been secured and Obenshain is well aware of that. “I tell my team, ‘You’re writing a chapter in the history of medicine’. The approval of Zynteglo and Skysona are key moments in that chapter.”

Leading The Flock

Obenshain has been involved in the gene therapy industry since he studied genetics, cell, and developmental biology at Dartmouth College, before receiving his MBA from Northwestern’s Kellogg School of Management. He has worked as a consultant, a venture capitalist, and then pursued a career in pharma by joining Genzyme and Sanofi in commercial roles before leaving to work in rare disease at Shire.

Having been a bluebird for many years, Obenshain – like his company - is indicative of the firm’s phenotype. He describes himself as non-hierarchical, collaborative, and mission driven. As a leader, he is clear on direction, adding that “people don't generally doubt what my opinion is on something.”

A visiting CEO once advised a younger Obenshain to plant himself where he would grow. Having planted himself at bluebird in 2016, his roots are now intertwined with the success of the company, as it continues to develop budding gene therapies. As an organization, those roots have created a company that is stronger than it was 18 months ago, and it is Obenshain’s leadership that will determine whether this plant now bears fruit.