HOW HALOZYME'S FIRST-TIME CEO FINANCED DRUG DEVELOPMENT

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ANYONE WHO HAS TAKEN ON THE ROLE OF PRESIDENT AND CEO OF A PUBLICLY TRADED BIOPHARMACEUTICAL COMPANY WILL TELL YOU IT'S CHALLENGING. DOING SO AS A FIRST-TIME CEO, WELL, THAT CERTAINLY ADDS TO THE DEGREE OF DIFFICULTY.

How about taking on the role as a first-time CEO in early January knowing you'll be presenting later that same month at the industry's biggest annual gathering, the J.P. Morgan Healthcare Conference (JPM)? This was the prospect facing Helen Torley, M.B. Ch.B., M.R.C.P., who was announced as the future president, CEO, and a member of Halozyme (pronounced halo-zyme) Therapeutics' board of directors on Dec. 17, 2013. "It's a bit like cramming for an anatomy test, as I needed to be capable of understanding and recalling a significant amount of factual information to be credible when answering investor and analyst questions," she analogized.

Dr. Torley met with Halozyme's leaders to learn what they believed were key opportunities and risks. She asked lots of questions, read stacks of documents and scientific publications, and gathered plenty of information. "From this I was able to put together a detailed yet facile Q&A with which I became very familiar," she shared. But she also wanted to be able to articulate her vision for the company, explain where opportunities resided, and craft an update of the corporate presentation to emphasize where she believed the focus of investors should be. Because while JPM 2014 was important, it was only one of about 10 investor conferences where she and then CFO David Ramsay would discuss Halozyme's future drug development potential, which to be realized would require a new strategy and a different approach to funding. "One of the first things I did was to focus the company," she shares. "We were working in drug delivery, dermatology, endocrinology, and oncology, and I decided we needed two central pillars." The first was ENHANZE, a drug-delivery platform rooted in the company's patented recombinant human hyaluronidase enzyme (rHuPH20). "It was not generating meaningful revenue at that time," she emphasizes. The second pillar was PEGPH20 (pegvorhyaluronidase alfa), Halozyme's asset in development for the treatment of pancreatic cancer. Torley's plan — grow revenue for ENHANZE to help offset the costs of investing in the company's proprietary drug development pipeline.

SHORT-TERM FINANCES FIRST — RESPONSE LETTER SECOND

After looking at the company's financials (see Table 1), she knew she had to figure out how to finance the company for the long term. Within a few weeks, the company raised approximately $115 million through equity financing. "A lot of investors were familiar with my performance as chief commercial officer at Onyx Pharmaceuticals [the position she held prior to becoming CEO of Halozyme Therapeutics], and I think this was very helpful in raising money to stabilize the company in those early days," she contends. "Making sure we had the money for staff and activities to build the business for the long term was a key initial step."

Torley next proceeded to look at the deals Halozyme had with other companies, including those with Roche, Pfizer, and Baxter, involving the company's ENHANZE platform. When the FDA had a ques-

TABLE 1: HALOZYME THERAPEUTICS ANNUAL PERFORMANCE

Year Ended Dec. 31	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016	2017
Net Income (loss) in millions	(9.1)	(13.3)	(14.8)	(23.9)	(48.7)	(58.4)	(53.2)	(19.8)	(53.6)	(83.5)	(68.4)	(32.2)	(103)	62.9

tion regarding Baxter's HyQvia (an investigational facilitated subcutaneous immune globulin product for use in patients with primary immunodeficiency), both companies received a complete response letter seeking additional preclinical data to support the biologic license application (BLA). "I quickly recognized that for us to be able to build platform deals to help obtain funding for our own drug development, there needed to be a clear pathway for approval of products involving our ENHANZE platform in the U.S.," she says. "Because while we had proven the platform in Europe with two Roche products, it seemed all other deal-making had stalled until we could get clear from this FDA complete response letter."

Having led FDA advisory panels and participated in many others, Torley became intent on getting to the bottom of the FDA's concerns. "I quickly took a key leadership role in preparing for the FDA's blood products advisory committee [BPAC], which was scheduled to meet in mid-2014," she attests. "We were at a make or break point for how big our ENHANZE platform could be in generating revenue for Halozyme, and the key to success hinged on getting through the BPAC."

COLLABORATION SUCCESS FAVORS THE WELL-PREPARED

In tandem with preparing for the BPAC, she also was expanding the company's business development team, so the company could sign and optimize future collaborations. She met with the BD, alliance leadership, and technical experts involved with deals that didn't happen to understand the barriers to success and to determine what could be done differently. "I'd ask questions such as, 'Did we have a meeting that included all of their key decision makers, including their head of CMC and head of technical operations? Was the head of clinical development ever involved in any discussion? Why or why not?' The group worked to understand the decision structure in each potential collaboration and ensure that all key stakeholders were engaged at the right time during the process and became much more proactive and strategic in collaboration building."

Part of that meant working closely with the collaborator's research, CMC, regulatory, commercial, and especially financial management teams. Torley stressed that all the stakeholders in a collaboration needed to be educated as to what ENHANZE is, what it would take for filing an IND, what would be involved in securing a regulatory pathway with the FDA, and so on. "Everyone needed to understand how using ENHANZE fit into their company's drug development strategy and the potential benefits it could bring. We needed complete buy-in to justify the financial terms, including the mid-single-digit royalty, because on some of these products that had the potential to be a fairly substantial number."

These deeper connections with the company's collaborators also helped Halozyme more thoroughly understand what was important to potential partners. For example, the time it took to get a drug into the clinic was a key metric in any collaboration. So, the Halozyme team looked at past data to see if there was anything that could've been done to speed up the process. One of the outcomes of this exercise was the development of the ENHANZE drug product (EDP). "For partners with Phase 1 studies wanting to get going more quickly, the program enabled them to mix EDP with their drug at the clinic site instead of going through a whole clinical supply manufacturing process to create a co-formulated product," she explains. "This approach shaved years off the amount of time it typically took to get into the clinic."

THE POWER OF FOCUS

When Helen Torley, M.B. Ch.B., M.R.C.P., joined Halozyme Therapeutics in early 2014 as the company's president and CEO, she soon implemented a two-pillar strategy, with one pillar being ENHANZE, the company's drug-delivery platform, and the other being PEGPH20, an asset in development for pancreatic cancer. "Internally, people liked ENHANZE and felt it worth pursuing, but I don't think they saw how big it could be," Dr. Torley contends. When asked how much internal resistance she encountered when implementing her two-pillar strategy, the executive replied, "The debate was more between diabetes and oncology."

Dr. Torley viewed diabetes as more of a niche play in a very expensive market. "I had been at Bristol-Myers Squibb and worked in diabetes for many years," she shares. "So, I was very familiar with the challenges and costs associated with launching a diabetic drug." For Torley, the business case of oncology versus diabetes seemed a no-brainer. That being said, when changing the company's strategy, it did take time and a few conversations to get everybody on board. "It's hard as a small company to try to be an expert in diabetes and oncology." But ultimately, everyone aligned, and she feels that opting to be two-pillar focused has helped Halozyme immensely.

People who know Torley well will tell you that she is all about focus. Being on some committees for BIO, there have been times when she has had to say, "These are all great conversations, but if we want to get things done, we need to focus on these two or three areas." Torley attributes her ability to focus in part to her medical training. "When I was a rheumatologist, I did a lot of emergency room intake of medical cases," she shares. "Doing ER triage, you have to quickly determine how sick the patient actually is. Is this an ICU case? Do I need to send them off for a cardiac cath? That type of stuff." According to Torley, medical training helps her define what's important versus what's a nice to have, as critical decisions need to be made fairly quickly. That being said, she also thinks her focus on focus is partly just how she's wired. "I am somebody who enjoys the details and likes to plan ahead of time," she laughs. "But I can't just look at a bunch of facts. I've got to put them in order and often say, 'Let's get a process here.'"

ENHANZE-ING HALOZYME'S DRUG DEVELOPMENT REVENUES

Torley's focus on the BPAC paid off. On July 31, 2014, the FDA's BPAC voted 15 – 1 that Baxter's HyQvia had a favorable risk/benefit profile. "I believe Janssen called us the next day to talk about it," Torley recalls.

According to Torley, Janssen was one of the first to recognize how having a sub-Q delivery could be a competitive advantage. On Dec. 17, 2014, Janssen and Halozyme announced their worldwide collaboration and license agreement for developing and commercializing products combining proprietary Janssen compounds with ENHANZE. Halozyme received an initial payment of $15 million, with the potential to receive additional payments upon achieving specified development, regulatory, and sales-based milestones totaling up to $566 million. Halozyme would also be entitled to royalty payments based on net sales of Janssen products using ENHANZE. "The Janssen deal represented a sea change for how people thought about our platform and served as a catalyst for a number of other collaborative ENHANZE deals," Torley asserts. For example, in 2015 Halozyme signed deals with AbbVie ($23 million upfront) and Lilly ($25 million upfront), both including milestone and royalty earning opportunities based on commercialized products. Halozyme has since entered into ENHANZE deals with Bristol-Myers Squibb ($105 million upfront), Roche ($30 million and $25 million upfront), and Alexion ($40 million upfront), all of which include milestone and royalty payment opportunities as well. In fact, based on the current and expected momentum of partner co-formulated products, Halozyme is projecting lifetime milestone potential of up to $1 billion and the potential for ENHANZE royalty revenue to approach $1 billion by 2027.

While Torley notes being slightly more involved in the Janssen deal (simply because Halozyme didn't have as robust a BD team at the time), she views her role as supportive. "I did coach our team and have occasionally gone to partner meetings when there was an absolute need or a missing capability," she clarifies. "But to suggest I'm the one who does the deals, well that isn't how it works. My teams are empowered, and all credit goes to them for the strong execution we've seen."

GOING AGAINST THE "CATEGORIZATION" GRAIN

"Are you a platform or drug development company?" This is a likely question often posed by investors and analysts to Torley because, of course, right now Halozyme is both, and that makes it difficult for those people trying to pigeonhole a company. "For the moment, there's a bit of a fad on VC-invested asset-centric companies," Torley notes. "But I believe the right strategy for Halozyme — certainly for the time being — is to be a platform and a drug development company, as we have synergies across both businesses that are important." Torley also believes such diversification provides Halozyme with a higher probability of success.

On the oncology side of the business, Halozyme is continuing to research its pancreatic cancer asset, PEGPH20. Torley says the company projects getting data readouts from HALO-301 (a Phase 3 global, randomized, double-blind placebo controlled clinical trial evaluating PEGPH20 as a first-line therapy for potential treatment of patients with metastatic pancreatic cancer) sometime in the second half of 2019. "That's going to be important in determining whether we continue to invest in the proprietary pipeline or increase our focus on ENHANZE," she shares. "Our investors know there is the potential for significantly higher returns if results for PEGPH20 prove positive. But in the meantime, we are delivering a lot of intrinsic value by having a growing ENHANZE business." In other words, Torley's two-pillar approach provides investors with a big potential upside while limiting the potential downside. "It also has made us less reliant on the capital markets, which is obviously very important," she adds.

Thanks to Torley's focus on ENHANZE, Halozyme Therapeutics was finally able to show a positive net income of nearly $63 million in 2017 (see Table 1), a company first since its IPO in 2004. "There aren't many companies of our size with two potential $1 billion pillars, and I like that." Further, thanks to the ENHANZE platform, Halozyme was able to execute a $150 million debt deal back in 2016. "We raised debt against future royalties from the deals we had done with Roche and Baxter, allowing us to keep the company capitalized in a less dilutive manner," the CEO adds. "The power of ENHANZE is many-fold, helping us weather whatever the financial markets are going to throw our way."