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Lilly Sings A New Tune: Chorus Unit Brings High Efficiency Note To Early R&D

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Lilly's independently operating Chorus drug development unit has created a means to mitigate the risk of drug development by conducting small-scale, targeted experiments separate from the larger R&D organization.

For the last three years, Chorus has been establishing itself as a wholly independent unit that essentially serves an internal outsourcing function for Lilly Research Labs: assets are transferred to Chorus for proof of concept work, which is done by an external network, and then returned to LRL.

"Chorus' efficiency derives from two principles - minimal infrastructure and small experiments," Chorus Chief Operating Officer Neil Bodick said in an interview with *"The Pink Sheet."*

By contracting with external experts and service providers, Chorus' "on-demand external capacity reduces fixed cost, and the use of external content expertise brings diversity and innovation to experimental design - the design of small experiments that absorb maximal risk is the core of our operation."

"And because we are clear about the style of investigation, it is possible to focus effort and to create a real sense of urgency," he added.

Lilly's Innovations On R&D Productivity

With the Chorus unit, Lilly is tapping into several recent trends that are part of the pharmaceutical industry's drive to improve R&D productivity. By creating a smaller, separate group and giving it control over a set of assets, Lilly has created a system to experiment with outsourcing and incorporating new methods, and maximize the return on its investments.

Lilly's experiment appeals to lean organizational principles, as well as big pharma's desire to act as a smaller organization. The group is intentionally small and designed to be nimble. Chorus' work processes can also more efficiently process early stage leads and get at go/no go decisions.

The Chorus business model is based on external alliances, relying on numerous outside contractors to outsource various operations rather than maintaining internal expertise in every aspect, as with traditional big pharma R&D set-ups.

Chorus also offers an arena for experimenting with cutting-edge methodology. Chorus is implementing new techniques and using new technologies, allowing them to modernize the development process and experiment with more efficient trial designs.

Perhaps most interestingly, Lilly has created a situation where it can experiment with some of its portfolio in this independent group, which is doing the testing of these new methods, insulating its larger R&D organization from potential failures.

"Throughout the last decade we've seen that increasing R&D productivity is a difficult task," Bodick noted Jan. 22 at *R&D Directions'* Drug Development Summit in Phoenix, during the first

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public presentation on Chorus. The creation of Chorus ties into that - it "was couched as an effort to increase productivity in early phase development," he told *"The Pink Sheet."*

Orchestrating Chorus - Creating A New Model

Chorus came out of e.Lilly, "an internal incubator set up to experiment with new business models." After a successful pilot, "the Chorus portfolio was enlarged and Lilly Research Laboratories (LRL) took responsibility for the funding on ongoing operations."

Bodick noted that Chorus is located at the University Hospital in Indianapolis - six miles outside of the Lilly campus. "That distance is there for a reason," he said.

Operations are largely autonomous, he explained, but portfolio objectives are aligned. Chorus' major interface with LRL is through the internal committee responsible for early phase development at Lilly.

One of the first steps in the Chorus experiment was to create a comprehensive computer model of a large R&D organization. Lilly contracted with Icosystems, a Boston-based strategy consulting company that analyzes complex organizational systems, and then used the model to "elucidate" various R&D processes.

For instance, the computer model was used to study how/where bottlenecks interfere with the development process. "It is to be expected that bottlenecks will emerge," Bodick said. "One of the interesting qualities that these models showed us is that these are very, very difficult to illuminate." By fixing a bottleneck in one place, "effectively you're creating a bottleneck in another place," he explained. "This is exacerbated by the flux in prioritization in portfolio management, [which] essentially sends ripples through the system."

Overall, what the computer models demonstrated was that "the team function matrix as an organizational construct does have a number of difficulties."

In setting up Chorus, Lilly tried to bypass the difficulties. "Around about 2002, we began to consider the development of an entire new kind of organization. We wanted to start with a clean slate," Bodick said. "What we wanted to do at the inception was to move drug development from the LRL mainstream into a network of external experts and service providers. We wanted to minimize infrastructure and develop software to take care of a lot of the complexity of managing the development process," Bodick said.

How It All Works...

Chorus focuses its activities on the early stages of development. It operates "between what we call candidate selection, the harvest of molecules from discovery, and clinical proof of concept - small Phase Ib, Phase IIa studies," Bodick said.

Since Chorus functions completely independently of Lilly, it is managing an independent portfolio. During the time that Lilly's compounds are transferred to Chorus, "all the decision making for the compounds within Chorus is within Chorus," Bodick stated.

The organization of Chorus was designed to reflect the cycle of work in early phase development, including a built-in ability to adapt. "New data essentially changes things," Bodick noted, so "[as] experiments generate new data, that will drive the cycle of planning. It's a very dynamic process." If the new data is sufficient to trigger a threshold for moving into another phase, Chorus has the flexibility to make that happen.

Chorus is organized around "a small core of experienced drug developers who are interacting with an external network of content experts," he explained. When a plan is mature, it is scheduled and "that same small core of drug developers interacts with a set of external service providers to do that experiment."

The small core consists of 24 FTEs, "15 of whom are senior scientists, so we're very heavily weighted toward senior investigators." The set of external experts that help with planning is called Alto, and the set of external service providers is called Bass.

Chorus uses the Alto network to gain specialized expertise and incorporate new methods into development plans. It currently consists of 45 experts who advise on topics such as experimental design; chemistry, manufacturing and controls; and drug delivery. The Bass network allows Chorus to farm out work to the participating vendors (at last count 72 service providers).

"For 24 people to handle 10 assets and 45 external vendors and the thousands of documents that are associated is a bit daunting," Bodick said. The way that is made possible is through specialized software designed for Chorus, called VOICE.

"VOICE is interesting in that it was really designed from our point of view as drug developers," Bodick said. It covers the entire range of Chorus' work, as well as creating a means to coordinate and interact with the Alto and Bass participants. VOICE includes work modules for planning, implementation, asset/portfolio management, financials and accountability. It also has a communication function; Bodick pointed out several messages on his Blackberry from VOICE alerting him to tasks he needed to do.

For Chorus, "a particular source of efficiency has been the minimization of infrastructure," Bodick said, noting that the VOICE software has helped in that area.

Another area of efficiency for Chorus has been its focus on narrow experiments and targeted questions, rather than broad, unspecific development programs. Bodick described it as "trying to cultivate truth-seeking versus success-seeking behavior."

In truth-seeking behavior, "the minimum experiment to discharge risk is selected and scale-up is deferred. In a success-seeking mode, scale-up is rapid with the assumption that program will be a success. Neither is correct in all circumstance, but the former is preferable when dealing with a large number of programs each of which has a relatively low probability of success," he told *"The Pink Sheet."*

Reviewing Chorus' Performance

Chorus has been able to significantly cut both the time and cost of development through proof of concept. Compared to a standard 40 months and roughly \$25 million, Bodick reported that Chorus has reached the "same amount of technical success in a year and a day with a total expenditure on the order of \$2.7 million." He added, "That's because we were only asking the key questions - that's truth seeking behavior."

Chorus started out with four assets in 2004. "We moved from there to 10 assets in 2006," Bodick said, and have managed 11 milestones in 2006. He described two positive proof of concepts that were achieved in 2006. For the first, an anticoagulant with a novel mechanism of action, Chorus was able to show POC in 74 patients, in 12 months and for \$2.7 million. The drug has been returned to Lilly's R&D portfolio.

The second was an analgesic with a new mechanism of action and poor delivery. "This was a languishing asset," Bodick noted. Because it did not get prioritization, "this was something that didn't go anywhere" at LRL. At Chorus, they showed POC using a "powerful surrogate marker" that was validated for central sensitization and associated neuropathic pain. "We demonstrated for \$3.12 million and 49 months that this had potential. It is now in Lilly's portfolio."

"We have returned a number of assets to LRL," Bodick said in the interview. "The successes immediately add value to the LRL portfolio, but efficient failure also has benefit and it is of note that the negative proof-of-concepts out of Chorus have not been resurrected."

Translating To A Larger Stage

The logical next step for Lilly is to adopt some of the lessons learned and processes established at Chorus for its larger research unit. Indeed, "those lessons are under active consideration," he said. However, during the presentation at DDS he also emphasized that scaling up the Chorus model for LRL will not be a seamless transition. "We have a lot of things to consider about how to advance this transformation," he cautioned. "We picked candidate selection to POC because it was a very clean area. ... As you move into a later phase, life gets more complicated."

In particular, Bodick pointed out that for later stage development, regulatory interaction and

connection to medical need will likely require "resident expertise and a larger dedicated team."

He suggested that Chorus could be most useful as a means of evaluating early stage compounds, allowing Lilly to capitalize on earlier in-licensing opportunities. "I think one of the really interesting possibilities is to use Chorus as the source of innovation, as a mechanism for in-licensing and quickly testing, and there are obviously great advantages to in-licensing prior to [POC] - you are all aware of what's happened to licensing fees for the last several years," Bodick said.

As well, Chorus "could be used to optimize value capture for LRL assets that are not in the strategic path for the organization, assets with value" that may not be within the scope of Lilly's operations, but could be explored by Chorus.

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