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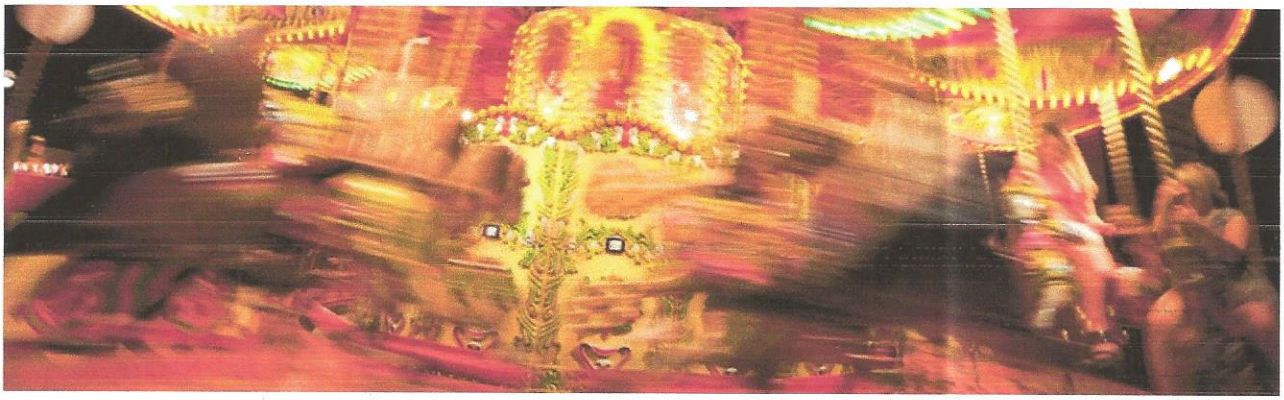

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R&D MERRY-GO-ROUND

WHAT R&D LEADERSHIP SWAPPING MEANS FOR PHARMA COMPANIES

BY ERIN MCCALLISTER, SENIOR EDITOR

An exodus of pharma R&D leaders to small biotechs and start-ups over the last year reflects a new phase in the ecosystem's churn of talent. But it's not all loss for the pharmas. The transition is expected to help them access innovation by improving the quality and number of in-licensing opportunities.

This year, 25 senior leaders in R&D from 17 different pharma companies have departed to take CEO or other senior management positions at smaller biotechs. Eighteen of those execs joined companies that were founded or raised a series A round in the last three years.

In contrast, only one has gone in the reverse direction. Hal Barron left biotech Calico Life Sciences LLC, where he was President of R&D, to join GlaxoSmithKline plc in January as CSO and President, R&D. Barron had held the Calico position since 2013; previously he headed up global product development at Roche.

The pattern reverses the trend during the last two decades when the flow of R&D leaders more commonly went into pharmas from biotechs or academia.

The change is largely due to the rich funding environment for new companies, which provides attractive resources for translating new technologies into products and delving back into the science.

Pharma leaders who are making the leap told BioCentury the hands-on access to research was a key part of the decision.

"In pharma, you rise up. You have the opportunity to take on greater and greater leadership roles and build organizations; those are wonderful opportunities. But it also starts to take you further

and further away from the actual studies, the science and the direct interactions with the treating physicians," Daniel Chen told BioCentury.

Chen was previously VP and global head of cancer immunotherapy development at the Genentech Inc. unit of Roche. In August he joined IGM Biosciences Inc. as CMO.

The moves provide biotechs with leaders who have experience bringing compounds from preclinical development to market, understand the regulatory environment, and can convey the value of their programs to investors.

"Scientific discovery isn't necessarily accelerating, but the relevance of that to human disease is changing."
Andrew Plump, Takeda

Pharma R&D leaders contacted by BioCentury saw the full half of the glass; they expect the shift of experience to biotechs will result in fewer missteps by the smaller companies, faster delivery of candidates, and more robust clinical programs than has been the case historically.

The churn is healthy for the ecosystem, the R&D leaders argue, because large companies will have a better supply of programs to in-license.

Still, most agreed pharmas could face a shortage of fresh blood at the top. Of the 25 slots the pharma-to-biotech transitions opened up, three were replaced by pharma-to-pharma moves, two were filled via internal promotions, and one was replaced from FDA. Three of the positions weren't filled at all because they were in therapeutic areas the pharma companies jettisoned. Replacements for the other 16 have not been disclosed.

The disclosed appointments show individuals with experience in clinical development rather than discovery are taking the top slots, reflecting the evolution in many pharmas towards focusing internal R&D on late-stage compounds, while relying on external innovation to fill the early pipeline.

Two companies are rethinking their top-down management structure to allow their R&D leaders to stay in closer touch with clinical research, without micromanaging. Takeda Pharmaceutical Co. Ltd. has an entrepreneurs-in-residence program, and Eli Lilly and Co. has structured its clinical programs into "biotech-like" environments, with that purpose in mind.

HANDS ON

This year, 168 companies have collectively raised about $5.3 billion in seed and series A rounds, a peak since BioCentury started tracking these numbers in 1994. Seven companies have raised more than $100 million each in series A rounds -- another high (see **"Super-sized Ambitions"**).

In addition, new technologies and targets in immuno-oncology, new modalities for multiple diseases, and discoveries opening up opportunities in autoimmune diseases are drawing pharma R&D leaders back to basics.

"Scientific discovery isn't necessarily accelerating, but the relevance of that to human disease is changing with a number of enablers evolving all over the world," said Andrew Plump, chief medical and science officer at Takeda. One enabler, he said, is "more and more capital being infused into the industry, and being infused even earlier."

The influx of VC cash gives biotechs the latitude to follow the science. "In some cases, there's lots of white space to let the science guide the company to where the opportunities are and focus on company formation rather than having to go out and raise money," said Douglas Williams, president and CEO of Codiak BioSciences Inc. Williams was EVP of R&D at Biogen Inc. from 2011-2015 before founding Codiak as one of the first exosome-based therapeutic companies.

Several R&D leaders told BioCentury the chance to create a company from the ground up satisfied career ambitions that the top position in a pharma didn't allow.

"In my case, it was the allure of a platform company with broad applicability and the ability to grow it organically from the beginning and build it to where it becomes a real engine for drug creation," said Williams.

"There are just more people who are interested in this translational space. For me, I thought of a start-up as a way to allow me to potentially help patients and foster my own enthusiasm," said William Chin, CMO at Frequency Therapeutics Inc. Chin joined Frequency in April from Pharmaceutical Research and Manufacturers of America (PhRMA), where he was EVP science and regulatory policy and CMO. From 1999 to 2010 Chin was SVP discovery research and clinical investigation at Lilly.

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Douglas Williams, Codiak Biosciences

For IGM's Chen, it was an opportunity to both manage a pipeline and interact directly with researchers. "In a biotech you can lead an organization, develop a strategy, be CMO, and at the same time you're running a Phase I trial you may also be interacting with physicians and analyzing the primary data," he told BioCentury.

That translates into faster decision making.

"In a small company, the transition of the ideas and thinking from the top to the bottom level is immediate," said Jeremy Levin, CEO of rare disease company Ovid Therapeutics Inc. Levin was previously CEO at Teva Pharmaceutical Industries Ltd. and SVP of strategy, alliances and transactions at Bristol-Myers Squibb Co.

Michael Vasconcelles, CMO at Unum Therapeutics Inc., agreed. "Sometimes it's really remarkable to me over the course of a week what we blocked and tackled through to make decisions." Vasconcelles was SVP and global head for oncology at Takeda from 2012 to 2015, when he joined Unum.

RECYCLING WITH PURPOSE

Pharmas are responding by filling the vacancies with leaders better equipped to take products through clinical trials than to explore the science.

"It used to be that the head of R&D was a top academic, typically a man who came in with a strong scientific reputation, who was very accomplished in an academic setting, but then had zero understanding of drug development," said Takeda's Plump.

Chen said many pharmas have found that's not the best recipe for the person tasked with building and running a pipeline. Nor is it necessary as the emphasis on external innovation grows.

"If you come from academia to industry, you've never run a clinical program or understood what it takes to collect data effectively and that ends up being a gap," said Chen.

"In a small company, the transition of the ideas and thinking from the top to the bottom level is immediate."

Jeremy Levin, Ovid

A view shared among the biopharma executives was that as pharma companies increasingly rely on biotechs for innovative programs to fill their pipelines, they are placing less importance on scientific prowess than drug development experience.

For pharma-to-pharma transitions, the hiring decision is often a proactive move designed to fit a specific need.

For example, Sanofi recruited John Reed, former head of R&D at Roche, as EVP, global head of R&D, filling the shoes of Elias Zerhouni who retired in June (see **"The Outsiders"**). In June, Daniel Skovronsky took over the role of SVP of science and technology, president of Lilly Research Laboratories and CSO at Lilly after Jan Lundberg retired.

"These pharma-to-pharma moves are all driven by different needs of the organization they're joining," said Plump.

Roche is the top oncology company by revenues; Reed managed the pharma's large oncology and immunology pipeline, as well as its CNS and infectious disease programs.

Reed's skills fit Sanofi's goal of competing in the areas of oncology and immunology (see **"Growing up Genzyme"**).

Skovronsky had managed Lilly's early stage research for four years before succeeding Lundberg. He also held senior roles in Lilly's tailored therapeutics division and served as VP of diabetes research. Lilly's pipeline has been dominated by next-in-class therapies. Of nine drugs launched since 2014, only one was first in class.

Skovronsky's new remit is to find first-in-class drugs with large effect sizes, which should allow him to draw on his background in early stage research (see **"Lilly's New Leaf"**).

Two outliers who came from outside pharma are GSK's Barron and James "Jay" Bradner, president of Novartis Institutes for BioMedical Research (NIBR).

At GSK, Barron is tasked with rebuilding the company's R&D pipeline, where he has decided to focus on immunology, including cancer immunotherapy. His years at biotech Calico, and earlier experience in the research-oriented Genentech division of Roche bring a science focus to the role.

"With Hal, you have someone who superbly understands oncology, understands areas of aging. Now that he's gone to GSK, he might find that he has the opportunity to exert that influence across multiple programs and that can be very exciting if you have a strategic view and can dive into doing new things," Levin said.

Bradner was an associate professor of medicine at Harvard Medical School, associate director of the Center for the Science of Therapeutics at the Broad Institute of MIT and Harvard, and a physician at the Dana-Farber Cancer Institute. He also brought entrepreneurial experience as co-founder of Acetylon Pharmaceuticals Inc., C4 Therapeutics Inc., Syros Pharmaceuticals Inc., Tensha Therapeutics Inc. -- now part of Roche -- and TetraLogic Pharmaceuticals Corp.

"He's a free-thinking oncologist with early expertise in drug discovery," making him a more atypical appointment for pharma, but well-suited to the position of leading NIBR, said Plump.

Barron declined to provide an interview; Bradner couldn't provide an interview in time for publication.

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Paul Peter Tak, Sitryx

Other academics are also continuing to enter the ecosystem, but mostly via positions in early stage research and start-ups. "When the science is still very early and has just come out of an academic lab, then the best person to run that on a day-to-day basis is someone with a better preclinical background," said Briggs Morrison, CEO and chairman of Syndax Pharmaceuticals Inc.

EXPERIENCED TO EXECUTE

Most leaders who spoke to BioCentury think the efflux of pharma talent will benefit the ecosystem. In particular, they say it will funnel experienced executives to biotechs, increasing the flow of innovative programs to feed pharma's late stage pipeline.

For the biotechs, seasoned leaders can move programs though the clinic or to an inflection point faster, and identify and jettison programs that won't be differentiated clinically.

"I know how to take it from Phase I to Phase III and the strategic considerations beyond that path in terms of what you really need to see to be considered maximal benefit for your therapy," Chen said.

"We're creating an ecosystem of biotech companies that can innovate, take multiple risks, and with leaders who will know if these programs look good enough that maybe they could become good pharma programs," said Paul-Peter Tak, former chief immunology officer and SVP R&D pipeline at GSK. Tak is co-founder of Sitryx Therapeutics Ltd., which launched on Oct. 8 with a $30 million series A round to develop immunometabolic therapies.

For example, the pharma mind-set should translate to more robust development programs, with multiple preclinical assays performed in parallel, allowing companies to deliver a larger portfolio of options for a potential pharma partner.

Morrison said having pharma ties will benefit biotechs for M&A. "If you have someone running the company who used to be an acquirer, you will have a good idea of what small companies need to be acquired," he told BioCentury. Morrison is former CMO at AstraZeneca plc. and an executive partner at MPM Capital.

Chen agreed, adding that the relationships former pharma execs bring can help during negotiations. "When it comes time to have a discussion about partnership or acquisition the pharma person is sitting across the table with someone who they have a relationship with. It's a person that the pharma leader has developed trust with."

But Tak thinks former pharma execs running biotechs could see beyond M&A more than is traditional in small companies. "One model you might see emerge from this is that some ultimately get made into a mid-size independent company like Alnylam," said Tak.

And according to Levin, the moves are seeding a long-term positive change.

"If you look in five or ten years from now, it will be extremely healthy because you will have established a common language between two segments of the industry," to help grow innovation and get those programs across the finish line, he said.

SATISFYING THE BIOTECH ITCH

Lilly and Takeda are taking active steps to create a culture that allows R&D leaders to stay in touch with the science.

Under Skovronsky, Lilly has organizations -- dubbed "trailblazers" -- that have independent budgets and boards of directors. They are structured to give the scientists freedom to pursue novel targets, with limited funding to induce a sense of urgency. Senior directors from outside these groups get the opportunity to interact with them and to cross-fertilize ideas between groups.

Takeda's entrepreneur-in-residence program has allowed the pharma to find and retain executives with an entrepreneurial leaning.

The program netted the pharma Stefan Wildt, now head of pharmaceutical sciences and cell therapy. After multiple roles at different pharmas, Wildt was interested in starting a biotech and began working via the EIR program at Takeda. The EIR program provides individuals with some financial backing and about 12 months to put a company together with access to Takeda's resources, including engaging with its researchers.

"With Stefan we started working with him and an academic to build out the company while he also served as a consultant to Takeda to build out its cell therapy unit," Plump said. The position of head of pharmaceutical sciences and cell therapy became available during that time, and both sides saw the fit.

Plump noted that pharmas also absorb employees from biotechs into less senior roles. They bring "energy and youth and when that flows into pharma, it sparks thinking in new and dynamic ways," Plump said.

He think it's inevitable that experienced executives will be drawn to biotech, and the best protection is to grow leaders internally.

"This transition we're seeing right now is good. But what's much healthier is to have a robust internal succession plan to avoid any talent gaps," said Plump.

COMPANIES AND INSTITUTIONS MENTIONED

AstraZeneca plc (NYSE:AZN; LSE:AZN), London, U.K.
Biogen Inc. (NASDAQ:BIIB), Cambridge, Mass.
Bristol-Myers Squibb Co. (NYSE:BMY), New York, N.Y.
Broad Institute of MIT and Harvard, Cambridge, Mass.
C4 Therapeutics Inc., Watertown, Mass.
Calico Life Sciences LLC, South San Francisco, Calif.
Codiak BioSciences Inc., Cambridge, Mass.
Dana-Farber Cancer Institute, Boston, Mass.
Eli Lilly and Co. (NYSE:LLY), Indianapolis, Ind.
Frequency Therapeutics Inc., Woburn, Mass.
Genentech Inc., South San Francisco, Calif.
GlaxoSmithKline plc (NYSE:GSK; LSE:GSK), London, U.K.
Harvard Medical School, Boston, Mass.
IGM Biosciences Inc., Mountain View, Calif.
Ovid Therapeutics Inc. (NASDAQ:OVID), New York, N.Y.
Pharmaceutical Research and Manufacturers of America (PhRMA), Washington, D.C.
Roche (SIX:ROG; OTCQX:RHHBY), Basel, Switzerland
Sanofi (NYSE:SNY; Euronext:SAN), Paris, France
Sitryx Therapeutics Ltd., Oxford, U.K.
Syndax Pharmaceuticals Inc. (NASDAQ:SNDX), Waltham, Mass.
Syros Pharmaceuticals Inc. (NASDAQ:SYRS), Cambridge, Mass.
Takeda Pharmaceutical Co. Ltd. (Tokyo:4502), Tokyo, Japan
Teva Pharmaceutical Industries Ltd. (NYSE:TEVA; Tel Aviv:TEVA), Petach Tikva, Israel
U.S. Food and Drug Administration (FDA), Silver Spring, Md.
Unum Therapeutics Inc. (NASDAQ:UMRX), Cambridge, Mass.

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