Visionary thought leaders such as Bernard Munos of InnoThink and the Milken Institute and Paul Stoffels, M.D., vice chairman of the executive committee and chief scientific officer, Johnson & Johnson, have been advocating for years that the blockbuster model is broken and unsustainable. They have been pushing for a change in the R&D model that will drive more transformational innovation. That day of transformation may be upon us, as small biotech and large pharma companies have started to work synergistically to create a faster, more cost-effective way to bring new treatments to market.

The short story is that small pharma brings nimbleness and a focused-approach to science that is uninhibited by the bureaucracy of large pharma, and large pharma provides the funding and the sales and marketing muscle to bring these innovative drugs to patients. This symbiotic relationship has proven to be a win-win.

This trend has been growing rapidly over the past five years within the industry’s R&D model. Gone are the guarded, years-long, high-cost searches for a blockbuster that was so common years ago for large pharma companies. Today, small pharma companies are overwhelmingly driving innovation, accounting for 63% of all new prescription drug approvals over the past five years. A report by HBM partners showcases this trend by tracking the NMEs that were originally developed by small, mid-sized, and big pharma companies. In 2009, small pharma was responsible for discovering 31% of NMEs; now jump to 2018, when 64% of all NME approvals originated from small pharma, a 103% increase over 2009.

Big pharma’s new role in this is to partner and fund the innovation that it so sorely needs to bulk up its dwindling pipelines. This is a cost-effective move for larger drug companies to leverage outside scientific talent to gain access to breakthrough discoveries.

“This is a dominant trend in the industry,” says Nach Davé, VP, development strategy, Premier Research. “Large pharma is deciding that rather than take the risk of developing a single drug over the course of seven to 10 years and spending $7 billion, these compa-
Emerging and innovative biotechs will decentralize the drug discovery pipeline and partner with larger pharma companies to develop breakthrough treatments that offer greater benefits beyond incremental improvements.

NAHEED KURJI
Cyclica

The industry has become more open-minded about its business model, and more companies are getting bolder and starting to implement new ways of doing business,” Mr. Munos says. “The pharmaceutical industry used to be built on proprietary knowledge, tools, science, and data. This has changed."

Innovation is now being energized by countless “mad scientists,” as Mr. Munos calls them, who work out of academia, incubators, or virtual companies.

“They add up to a giant grassroots innovation movement that operates on a shoestring,” he says. “Together, they explore emerging biology, and are quick to embark on translation when they spot an opportunity. It used to be that a biotech startup would need $50 million to get going because it had to recreate all the functions of a big company — HR, legal, and everything else. Today, companies don’t need this type of infrastructure. They can turn to crowdsourcing platforms, like scientist.com, for example. So, if you’re a chemist you focus on chemistry and procure everything else from the crowdsourcing platform when you need it. This flexibility has changed the dynamics of innovation. Startups now have the opportunity

In 2018, a team of researchers at MIT, led by J. Christopher Love, Ph.D., engineered a miniaturized biopharmaceutical factory that could fit on a dining room table and produce hundreds to thousands of doses of a needed treatment in about three days.

As published in the journal Nature Biotechnology, this on-demand manufacturing system is called Integrated Scalable Cyto-Technology (InSCyT). It is fully automated and can be readily reconfigured to produce virtually any approved or experimental vaccine, hormone, replacement enzyme, antibody, or other biopharmaceutical. With further improvements and testing, InSCyT promises to give researchers and healthcare providers easy access to specialty biologics needed to treat rare diseases, as well as treatments for combating infectious disease outbreaks in remote towns or villages around the globe.

The researchers report that it took them about 12 weeks to devise the processes needed to produce each drug. That’s compared with a year or two that is normally required to get a more traditional, large-scale manufacturing operation up and running.

Source: NIH Director Dr. Francis Collins, NIH Blog
When large pharma started to turn its attention to smaller companies, innovation finally had a stage and an opportunity to be accelerated.

NACH DAVÉ
Premier Research

The more people engage in innovation, the more ideas, hypotheses, and drug candidates will get into the clinic.

BERNARD MUNOS
FasterCures, a Center of the Milken Institute

Small Pharma

Pharma Spinoffs Spur Innovation

In addition to funding innovation from outside sources, sometimes large pharmaceutical companies create their own spinoffs to discover and develop innovative products as an independent arm of the larger business. This model may operate differently from an independent startup, but there are many advantages over the cumbersome R&D model of big pharma.

“Now, there is another player that has come to the table and that is large pharma, which has very deep pockets,” Mr. Davé says.

According to Mr. Kurji, large pharmaceutical companies are definitely supporting the creation, early-stage investment in biotech companies through their venture arms, but he also sees the venture capital ecosystem warming up to small pharma.

“Early-stage biotech companies are seizing the opportunity to grab their share of the market, with recent data from IQVIA suggesting that emerging biotech companies now account for more than 70% of the total R&D pipeline, up from 52% in 2003,” Mr. Kurji says.

“Emerging and innovative biotechs will continue to decentralized the drug discovery pipeline and develop breakthrough treatments that offer greater benefits beyond incremental improvements and reshape the way medicines are discovered and brought to market.”

Funding Gets Easier

This emerging paradigm makes it easier for small or emerging companies to get funding, whereas before it was one of their biggest hurdles.

When small biotechnology companies had to rely on venture capital only, funding was difficult. If the VC-driven environment lost confidence in the biotechnology space or if fund managers lost confidence in certain medical innovations then the money stopped flowing in.

“Now, there is another player that has come to the table and that is large pharma, which has very deep pockets,” Mr. Davé says.

“So, when a VC will not fund an innovative company or innovative product, these companies have at least another suitor that can fill that gap — big pharma.”

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There has been considerable interest in the small pharma and biotech industry, which has certainly captured the attention of VCs,” he says. “StartUp Health in its Q3 insights reports that there has been a considerable increase in both the funding amount and deal counts in the healthcare and pharma space. In 2010, there was $1.1 billion with 152 deal counts, which is in stark contrast to the $10.4 billion and 556 deals by Q3 of 2019, with the largest amount of funding focused on earlier stage healthcare companies.”

Not only has there been an increase in the number of deals and funding, there has also been an increase in the pool of investors supporting smaller biotechs and healthcare companies, with 1,061 unique investors participating in the industry, compared with 299 in 2012.

A large proportion of these investors are based in the United States, and most venture investments are focused around companies in Silicon Valley and Boston. There also has been recent growth in the Asian markets, particularly in China.

“As the market evolves, we will see a greater decentralization of resources as big pharma, non-profit organizations, and venture capital firms seek further innovation opportunities,” Mr. Kurji says.
Emerging Company Trends

Emerging biopharma companies account for 72% of all late-stage pipeline activity, up from 61% a decade ago. During the next five years, trial productivity will be heavily influenced by 8 key trends, according to an IQVIA Clinical Development Trends Impact Assessment.

1. Digital health technologies will enable the capture of drug efficacy and safety data remotely, which can improve patient safety, enable virtual trial formats, and ease site work burden.

2. Patient-reported outcomes will shed new light on patient experience and drug efficacy and safety outside the clinical setting and lead to accelerated trial times as endpoints shift.

3. Real-world data will optimize trial design, speed investigator and site selection, and enable new trial designs by acting as virtual control arms and supporting pragmatic, adaptive, and RWE registry trials.

4. Predictive analytics and artificial intelligence will identify new clinical hypotheses, reduce trial design risks and speed enrollment by identifying protocol-ready patients.

5. Shifts in types of drugs tested, for instance, to targeted therapies and next-generation biotherapeutics that improve efficacy and success rates and have accelerated development timelines but require longer-term patient follow-up.

6. Biomarker testing availability to help narrow patient populations to those more likely to see effect, resulting in improvements in efficacy, safety and success.

7. Regulatory landscape changes will encourage the adoption of precision medicine approaches, novel trial designs, and endpoints while providing means for accelerated drug approvals and regulatory success.

8. Pools of pre-screened patients and direct-to-patient recruitment will facilitate enhanced trial enrollment, shortened trial duration, and faster market availability.

Source: IQVIA Institute for Human Data Science Study

financially support the ideation and creation of new companies that are strategically aligned to the pharma company’s mandates.”

While the hurdles that independent startups face are much higher than those of pharma spinoffs, there are advantages to being independent, he says. “An independent startup has more freedom to operate and try new things and pivot along the journey,” Mr. Kurji says.

Mr. Davé says the incubator concept within large pharma started gaining ground about three years ago.

“Large pharma companies started to create their own incubators and attract talent to those incubators,” he says. “I’ve seen many cases where top scientists from the academic space have shifted over to large pharma incubators where they’re still doing the same thing but the opportunities to advance their science and technology are better, because of the infrastructure that a large pharma company can provide.”

Many large pharma companies have started to move in this direction, realizing that it was a way to thrive and prepare for the transformation that is taking place in the industry.

“I’d say half of the top 12 pharma companies have a pretty good understanding of what’s going on,” Mr. Munos says. “They started long ago to prepare themselves for the transformation that is taking place. For instance, I remember when I first met Dr. Stoffels 10 years ago he would tell anyone who cared to listen that the model was broken and needed changing.”

Not surprisingly, years later, Dr. Stoffels was instrumental in developing JLABS at J&J, which now comprises 12 pharma startups which are mentored but not funded by J&J, according to Mr. Munos. “This allows JLABS to explore emerging biology in 400 directions, something that could never be done within the company because it would raise its risk profile to unacceptable levels,” he says. “But the purpose is to unleash innovation and it is working great guns.”

Mr. Munos also notes that Novartis, AstraZeneca, Bayer, Takeda, Boehringer Ingelheim, and Merck KGaA have retooled themselves in ways that have re-energized innovation.

The round up in his own words: “Novartis has gone through various iterations or versions of its innovation model. This was one of the first companies to return to scientists the freedom to innovate and the company has become one of the most prolific innovators, with 20 drugs approved in the last 10 years. AstraZeneca had a difficult transition, but its new drug output is rejoining the company to the leading innovators. Interestingly the mid-size companies such as Bayer, Takeda, Boehringer Ingelheim, Merck KGaA, seemed to have felt the heat a little sooner than their larger peers. But they all came to the realization that they needed to act in order to thrive in the new environment and they came up with new innovation models that have been remarkable. Takeda is a prime example of what we’re discussing because it used to be a rather staid company. Likewise, Boehringer Ingelheim came up with its own approach after realizing that much of the high-value innovation comes from outside. So it created a "research-beyond-borders" model that aims at harnessing new innovation ripples before they become waves. And its leadership has been pretty savvy at doing this. And Merck KGaA has taken multiple initiatives to basically implement open source R&D within its corporate structure.”

“All this is taking place as we speak and it is changing the dynamics of research by booting new drug approvals while harnessing the shoestring economics of startups,” Mr. Munos continues. “Basically, this is opening pathways to overcome the pricing and affordability challenges that companies have been facing. It is putting the industry back on a sustainable course.”

“When large pharma companies started to turn their attention to smaller biotech and emerging companies, innovation finally had a stage and an opportunity to be accelerated,” Mr. Davé says. “While we’re not producing $1 billion drugs, we are producing many more drugs that are providing solutions to a wider range of patients who were ignored or unattended to from a therapeutic perspective. Large pharma’s shift in focus away from billion-dollar drugs to more innovative drugs has proved beneficial to patients.”

With more companies and people engaging in innovation, there will be more ideas, more hypotheses, and more drug candidates that make it to the clinic. Scientific breakthroughs are quickly followed by the creation of multiple well-funded startup companies to exploit the new opportunities.

“This wasn’t the case 10 years ago, but now it’s become routine,” Mr. Munos says. “The reality is that if innovation is getting cheaper, we’re going to see more of it, and that’s exactly what is happening.”

Mr. Munos adds this as a “very exciting time” in the industry and there are many reasons to be optimistic about the future of the pharmaceutical industry. He anticipates that entrepreneur scientists and small companies will have a much easier route to achieving their goals than they have in the past.

“There will be a lot of turbulence in the near term, but in another five to 10 years or so, the industry will be on much better footing,” Mr. Munos says.