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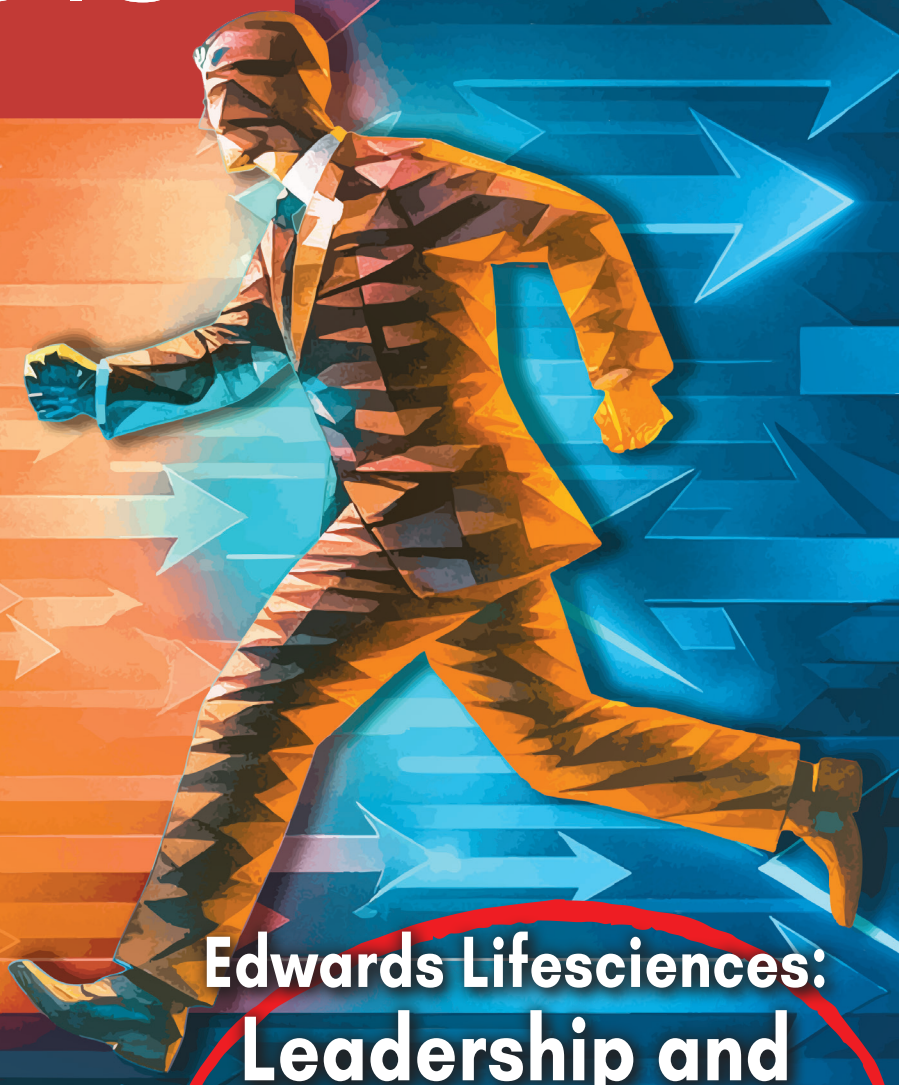

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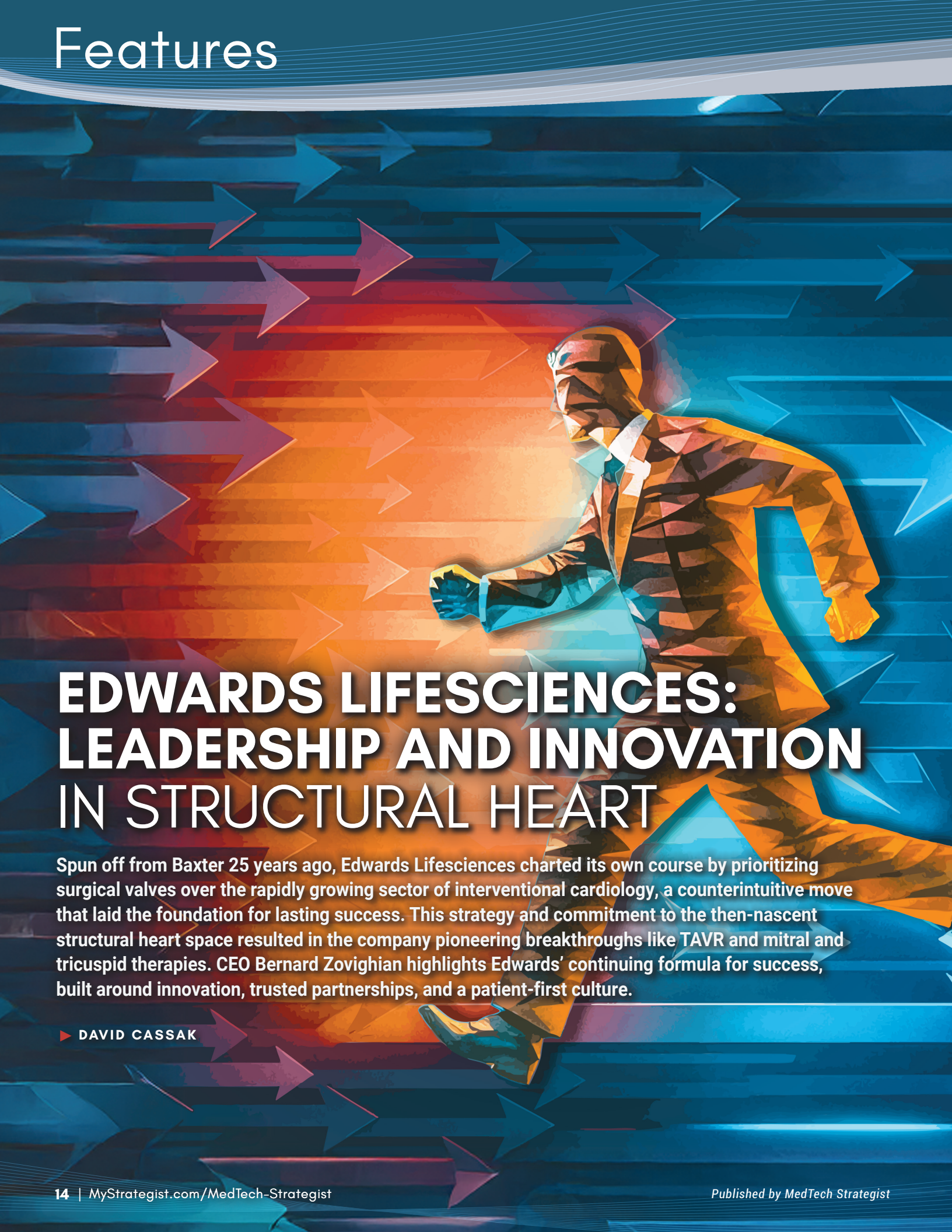

EDWARDS LIFESCIENCES: LEADERSHIP AND INNOVATION IN STRUCTURAL HEART

Spun off from Baxter 25 years ago, Edwards Lifesciences charted its own course by prioritizing surgical valves over the rapidly growing sector of interventional cardiology, a counterintuitive move that laid the foundation for lasting success. This strategy and commitment to the then-nascent structural heart space resulted in the company pioneering breakthroughs like TAVR and mitral and tricuspid therapies. CEO Bernard Zovighian highlights Edwards' continuing formula for success, built around innovation, trusted partnerships, and a patient-first culture.

DAVID CASSAK

When **Edwards Lifesciences** spun out of Baxter in 2000, it was not among the pantheon of cardiovascular medical device giants that built huge businesses in the 1980s and 1990s based on the rapidly emerging field of interventional cardiology, driven by coronary stents—among the rare device blockbuster products. In the quarter century since then, however, Edwards has soared to a leadership position by adopting what, by any measure, can truly be termed a contrarian strategy. The company parlayed its leadership in surgical heart valve replacement into a leading position in the then-nascent structural heart space driven by its pioneering efforts in transcatheter valve replacement (TAVR) on the back of its 2004 acquisition of TAVR pioneer Israeli-based start-up Percutaneous Valve Technologies (PVT).

Turning your back on your core customer base, which for Edwards was surgeons, in favor of a still-yet-to-be established specialty (interventionalists) is generally considered a formula for failure. But it has worked incredibly well for Edwards, not only in driving the company to a leadership position in structural heart, which has emerged as a significant cardiovascular market, as interventional cardiologists have also become a dominant specialty, but also in driving shareholder value. The retirement of long-time CEO Mike Mussallem (who ran the company since the spin-off) opened the door to a new leadership team atop Edwards, which tapped long-time company veteran Bernard Zovighian in 2023 to steer Edwards in its next major growth phase. Zovighian joined Edwards in 2015 to run the structural heart business after 20 years with Johnson & Johnson. In the following interview, Zovighian discusses what has made Edward so successful and where the company is headed from here. (*See also, "TAVR Update: Market Leaders Medtronic and Edwards Look to Conquer New Indications and Solve Old Problems,"* MedTech Strategist, *September 4, 2024.*)

Medtech Strategist:* *I've been writing on Edwards since soon after the spin-off from Baxter. At that time, Edwards was somewhat of a contrarian in the cardiovascular space. It was the dawn of interventional cardiology and while most of Edwards' peers in big medtech, such as Guidant, Johnson & Johnson, and Medtronic, were making major moves into interventional cardiology, Mike Mussallem [the CEO at that time] was adamant that Edwards stick to its knitting.

Edwards was a cardiac surgery company with some adjacent product offerings in mostly older technologies and it didn't want to get into competition with those other large players, it wanted to serve its surgeon customer base, and was worried that to a certain degree a move into interventional cardiology would have been perceived as turning its back on its core customers because surgeons and interventionalists were quite competitive at the time, particularly when it came to bypass surgery. Is that a fair reading of what Edwards' strategy was at the time?

BERNARD ZOVIGHIAN

Bernard Zovighian: Yes, that's a good way to think about what our strategy was 25 years ago. We were a surgical company, and many years earlier had introduced the first artificial heart valve based on the work of Dr. Albert Starr and Miles "Lowell" Edwards. As part of that, we have been a leader in surgical innovations for more than 65 years. And it wasn't easy to change at the time. We maintained our focus on cardiac surgery while others were pursuing interventional cardiology. We took care of the surgeon and the patients who most benefited from surgery, and that's still the case today. As a result, we are the company with the broadest, most comprehensive pipeline in cardiac surgery.

But it was still mostly about aortic valves at the time.

Yes, though we've continued to innovate over time and also added a surgical mitral valve and repair technologies. As a matter of fact, 65 years later, we're still the leading innovator in the cardiac surgical space.

That said, if you look at our revenue today in surgical, most of it comes from the technology that we introduced in the last five years, including the most durable heart valve available today, *INSPIRIS* with our proprietary cutting-edge *RESILIA* tissue technology. I'm proud to say that we've taken care of both our legacy business in cardiac surgery and, at the same time, 20 years ago we evolved into interventional cardiology through pioneering innovations of our transcatheter technologies, like TAVR.

> "When we think about innovation at Edwards, we aren't just thinking about next year or the next quarter, we're thinking longer term, as well: can we change the practice of medicine?"

Evolving into interventional wasn't easy—there was natural competition both internally and externally—but as I look back, I believe we did a very good job. I believe the leadership and innovations we've continued to bring to patients with structural heart disease makes Edwards one of the best success stories in medical technology.

Today when I visit any healthcare systems in the US, Europe, or anywhere else in the world, we are clearly recognized as the leader in cardiac surgery and TAVR, but now that includes mitral and tricuspid. I think that's quite amazing.

When you talk about cardiac surgery, you're referring mostly to valves not unclogging arteries as a procedure?

Correct, we're really all about structural heart, so primarily the valves.

I might add parenthetically that about 30 years ago when I was doing an article on Edwards, I was invited to watch as someone who just had an Edwards valve implanted was brought in to meet the person who actually assembled the valve. That was a time when most devices came out of a sterile package and here they were, hugging the person who effectively saved their life.

And we still do that today with patients and our employees around the world. It's a very moving moment, not just for the patient, but also for our employees. Our patient-focused culture we live and breathe at Edwards truly comes to life at these events we call The Patient Experience. We hold these events around the world, and the stories we hear from patients and care partners are instrumental in helping us develop our innovative technologies and transform care pathways for patients. In the end, it's what I love about what we do: we take care of people.

Let's talk about your career. You came to Edwards from J&J. Did you come from Cordis or some other operating company because I know the stent came in through Ethicon, around that time. What were you doing for J&J at the time?

I spent about 20 years with J&J. I was in New Jersey at one point, but also Europe, Canada, and California. I basically grew up most of my time within Cordis and the cardiovascular division of J&J in different functions and different locations over 20 years.

J&J is a large healthcare company, and I learned so much—when I look back, what I learned the most is the process of running large-scale operations. I've been very fortunate to have been with two world-class companies, J&J and Edwards.

Let's talk about Edwards' innovation process, which as you described, has been the key to the company's success.

When we think about innovation at Edwards, we aren't just thinking about next year or the next quarter, we're thinking longer term, as well: can we change the practice of medicine? Can we bring breakthrough solutions to patients in the next 10 years? And we're committed with big investments in important innovations. Edwards really takes the innovation process to another level.

The interesting thing about that is, at one time, no one would have pegged Edwards as a leader in innovation and a candidate to be arguably the dominant cardiovascular device company in the first quarter of this century.

Well, I see what you're saying. But Edwards has been the leader in structural heart since the company was founded over 65 years ago. We've never been the biggest medtech company, but we've always been and still are the leader in structural heart. And it didn't happen by accident. It starts with our credo and our culture and how we prioritize our patients. We prioritize innovation, and the investment and agility around that. Sustainable growth is an outcome of our unique innovation strategy.

Am I right in thinking that from a financial or investor perspective, Edwards has been one of the best performing public medtech companies over the past decade or so?

Edwards has performed well financially over the past 10 years. There are always fluctuations in the stock market quarter over quarter, but we spend more time looking forward than looking

backward. We believe that by continuing to bring meaningful innovations to patients and physicians, we'll deliver differentiated financial results as well. That approach has guided us since our IPO 25 years ago, and it continues to shape our strategy today.

We know now that TAVR is a huge success. Can you give us an assessment of what you think the potential of the mitral and tricuspid technologies are? There are some people who think the transcatheter mitral valve opportunity is actually bigger than transcatheter aortic just because of the different sizes of the two patient populations.

Exactly. Let me begin by talking a little about the complexity of this innovation and then about the size of the opportunity. As with TAVR, we had launched a mitral program about 15 years ago that we worked on for three or four years. But it wasn't ready.

Were these all internal development programs?

Yes, then we bought a company called CardiAQ that had developed a second-generation technology, and after the acquisition, our engineers took the learnings from our internal program and came up with a third-generation device. Today that's the *EVOQUE* technology for tricuspid patients and it is an amazing success. It represents 15 years of development and commitment by our world-class engineers and hundreds of millions in investment. The key is to have the vision and the long-term commitment to find the most impactful innovation for those in need.

Is mitral valve disease a condition similar to aortic valve disease, or is it totally different? Is there a lot of synergy between mitral and aortic, or are they really two very different things?

They are two different things. If you look at aortic, our *SAPIEN* platform can treat most of the patients with aortic stenosis. However, the anatomy and the complexity of the disease is different on the mitral side. Also, the needs vary by patient. Therefore, one technology is not going to be sufficient.

To address that, we've developed a toolbox with a few different technologies and modalities including repair and replacement. We just had one approved in Europe, *SAPIEN M3*. All of which is part of our strategy—eight years ago, we anticipated the promise of the mitral valve opportunity and said, "Let's make this happen as there are so many patients in need." And from the beginning, we said that we want to be the leader and create this category by bringing the best solutions for patients. We believe the mitral opportunity is going to be significant. There are at least as many mitral regurgitation patients as aortic stenosis patients, maybe even more, and yet there are very few options for them today.

People have been debating the size of mitral and tricuspid markets for a while now. Do you have a sense of whether the market is developing the way you thought it would and what's the key to that? Is it technology driven or customer driven?

It's a little bit of both. We need to develop great technology and generate high-quality clinical evidence so that physicians are confident that they're really helping their patients. We also need physician training, and we need to ensure access through coverage and reimbursement.

We have an important role, but it is a role that we know how to play. We've done it in cardiac surgery for the past 65 years and we've been doing it in TAVR for the past 20 years with profound impact to more than a million patients around the world. We believe our mitral and tricuspid transcatheter therapies will be another success story, just like cardiac surgery and TAVR.

Edwards has grown through both internal development and acquisitions, and 2024 was an extremely busy year for Edwards in terms of M&A. You announced the intention to acquire JenaValve, JC Medical, and Innovalve. Where do they fit in the portfolio that you're building in the transcatheter valve space? Are they mitral valves or aortic?

Before I go there, I'll give you a little bit of a sense about why we did these acquisitions. When I took over as CEO a little more than two years ago, we spent time reflecting on how we continue to be successful over the long term, and we came to a couple of conclusions: one is that our foundation should remain the same and our commitment to innovation should remain key. The question that raised is, did we have the right portfolio for the future?

At the time, we had TAVR, cardiac surgery, mitral, and tricuspid. And the realization was that we could do more, while remaining focused on structural heart. Aortic regurgitation [AR] is a natural progression of that—it's a deadly and progressive disease that affects a significant and growing number of patients, many of whom currently have limited treatment options. Do we want Edwards to do anything there? Absolutely. Therefore, we announced the intention to make two acquisitions—JenaValve and JC Medical—with the goal of leveraging our innovation capabilities and world-class science to accelerate the availability, adoption, and continued innovation of life-saving treatments for patients suffering from AR.

Innovalve is a mitral valve that will be part of our TMTT business [transcatheter mitral and tricuspid therapies]. The Innovalve transaction was appealing to us because it brought us, even if early stage, a truly disruptive technology for mitral patients. Our *M3* internal platform and Innovalve have the potential to expand the mitral patient population.

We also acquired Endotronix as part of the newly formed IHFM [implantable heart failure management] group.

JenaValve has been around for a while and may be familiar to people, but Innovalve is an emerging company. What is the background of that deal?

They're a start-up based in Israel. It's very early stage. So they'll probably need several more years before achieving a US approval. We'll have to put our innovation engine behind it, but we believe the concept is very innovative, which is why we made the acquisition. With the goal of being able to treat even more patients with unmet needs with both platforms, *M3* and Innovalve.

Did Edwards have its own internal development programs in mitral and tricuspid the way it did in aortic?

Yes, and we just got approval in Europe for the world's first transfemoral transcatheter mitral valve replacement system [*SAPIEN M3*]. And we're on track for US approval next year.

Do you see M&A as a critical strategy going forward for Edwards in terms of creating the pipeline it needs and customers want?

Yes, but no more than in the past. We were and continue to be investors in early-stage companies.

Were these investments or acquisitions?

Both. When we make an early-stage investment, we typically put our engineers together with that company's engineers to collaborate for several years to help develop a first-generation technology.

Are you now confident that your profile in the start-up community is high? I mean, are you getting more opportunities just because of all the success you've had so far?

Yes. I think because we are one of the few strategics that invest early. Don Bobo [CVP of strategy and corporate development] and Todd Brinton [chief scientific officer and CVP of advanced tech] are talking to, in any year, many early-stage companies in structural heart. When we see potential, we invest early. In certain situations, we may take a Board seat. If, after a few years, we like the progress and see potential to impact the healthcare ecosystem and patient care, we may enter into a more formal agreement.

Do you have a set budget for investment? Or is it serendipitous, where as you find an attractive technology, you go for it?

We have an internal team, and we meet on a regular basis to talk about new companies and developments and provide updates on previous investments the company has made. In that way, we stay very close to the innovation that's happening in the structural heart ecosystem. As I mentioned before, whether it is developed in-house, through investment and acquisition, or a combination of both, our constant innovation drives patient care, especially with early-stage or unmet patient needs.

At our Bohemian conference held last year, both Todd and Don were on a panel, and they made the point that Edwards' next major move is to become the leading player across the full spectrum of structural heart. What can you share with us about that ambition and how structural heart represents a new and logical opportunity for Edwards as opposed to just a subset of the valve business?

It's very much aligned to the reflection I shared about when I became CEO. We were already the leader in cardiac surgery, TAVR, mitral, and tricuspid. And then the question was, what other patients' needs in the structural heart space could we address? And we said, as a company, we need to bring innovative solutions to the many structural heart patients in need. We already spoke about AR. Let me share a bit about structural heart failure.

Structural heart failure is a natural part of our structural heart focus and a meaningful progression for us. It's a large opportunity with significant unmet patient needs. Millions of patients with no solution. These patients' quality of life can be unbearable. So we are looking at multiple modalities to help these patients.

Do you envision your growth in that space will come through a similar combination of early-stage investing, and acquisition or internal development that worked so successfully in TAVR?

We'll do it the same way. Some will be internal development, and some will be through investments and acquisitions. As an example, we recently acquired Vectorious, a company developing a miniature implantable pressure sensor that we believe can further transform the management of heart failure as part of the IHFM portfolio. Right now, we're spending 17-18% of revenue on R&D every year, which amounts to about a billion a year across early stage, mid stage, and late stage.

Back in the day when Edwards acquired PVT, there were a lot of venture-backed companies trying to jump on the

transcatheter valve opportunity. Is there the same kind of busy landscape in heart failure and structural heart in terms of investment?

Yes, there are many, but the way you phrased the question is interesting because at the time of the PVT acquisition, Edwards was a different company, much smaller than we are now, so we did that one transaction and then not another for a while. Today, we are a much more established company and able to invest a lot more in R&D. We're taking a portfolio approach recognizing that early-stage innovations have risk and might not be successful.

Do you have any strong feelings about whether you'd rather take an equity stake in a small company leading to an acquisition? Or, given Edwards' own ability to develop new devices, pursue innovation through internal efforts? Is either path more attractive to you?

We don't have any preference because in most cases it's a combination of internal and external, but our goal is very clear. We want to have the best technology and bring the most value to patients, physicians, and health systems. It is truly about having a different kind of impact on society. At the end, our innovation enables competition. By developing and leading, others are incentivized to follow quickly with additional technologies or advancements to existing technologies, and that is good for patients.

As you scan the landscape, how close do you think you are to that goal of being a category leader in mitral and tricuspid? And as you look to your next challenge, does your success in TAVR help in your goal to be a leader in heart failure and structural heart?

I think so because of our reputation, focus, and expertise within structural heart. It is widely recognized by all stakeholders—patients, trusted physician partners, and the larger healthcare ecosystem.

Edwards brought Todd Brinton in a couple years ago to run what you're calling the Advanced Technology group. What is the synergy or relationship between Todd's group and what Don does in Business Development?

Together, they collaborate to support our innovation strategy. Don leads two major functions for the company: Strategy and Business Development. Todd also has two key responsibilities: nurture innovation inside Edwards that is not currently part of our business, and he provides clinical and medical assessments of technologies we are evaluating for investment. Todd also lends his expertise as an interventional cardiologist to help reinforce our leadership in shaping policy that expands access to breakthrough structural heart innovations. He recently testified for the second time before the House Energy and Commerce Health Subcommittee, spotlighting the urgent need to modernize coverage pathways, which is critical to ensure patients have access to life-saving therapies, and aligns closely with other important policy and access work we're engaged in globally.

> "Right now, we're spending 17-18% of revenue on R&D every year, which amounts to about a billion a year across early stage, mid stage, and late stage."

J&J made a major acquisition last year when it acquired interventional ultrasound company Shockwave and Boston just announced that it's getting into interventional ultrasound. Given Todd's role as one of the founders of Shockwave, should Edwards have been the buyer of Shockwave? Was that something that you guys talked about?

We're a structural heart company. We review all opportunities within structural heart, and we apply our own filter to decide if it's the right fit. Some of that consideration includes [asking] can we be differentiated? Can we truly help bring value and help many patients? And if the answer to any one of them is "no," we don't go any further.

Do you envision this as a long-term strategy? If we have this conversation in 25 or 30 years, do you think the Edwards story will be about the acquisitions you've made in the last decade and the seeds planted when you started to do all this acquisition and investment?

I hope our DNA will remain the same because we are so differentiated and it is working well. Our innovations provide value beyond the delivery of care, providing long-term patient benefits. This provides impact beyond the individual patient, expanding to health systems, to communities, and to society.

> "I hope our DNA will remain the same because we are so differentiated and it is working well. Our innovations provide value beyond the delivery of care, providing long-term patient benefits."

No small part of what makes the Edwards story so interesting is where the company came from and where it stands today, from a company spun off from Baxter pursuing mostly surgical and lower-tech product lines, to a leader in structural heart innovation. I will say again, just from my long perspective on Edwards, the notion 30 years ago, that anyone would make the argument that Edwards would become an innovation and market leader in a very competitive cardiovascular industry would not have been taken seriously by most industry observers. I'm not sure a lot of people understand how significant the company's evolution over the past 25 years has been.

Exactly. And we continue to evolve. Not just in the areas we've discussed, but also in building high-quality scientific evidence. The most recent example is our EARLY TAVR trial. Last year, we presented the findings of a large study on asymptomatic severe aortic stenosis patients, essentially patients who have severe disease but have not yet developed symptoms. The data showed that waiting for symptoms for some patients is not an effective strategy for the management of this complex disease. Without treatment, 1 in 10 patients experiencing symptoms may die within five weeks. However, these symptoms can be difficult to detect and may progress rapidly and unpredictably. The data underscored the importance of urgently referring patients to a heart team to be evaluated once they get the diagnosis, even if they don't yet have symptoms.

It also brought a renewed focus with the clinical community to streamlining the management of patients with severe disease, enabling closer follow-up and more timely treatment of patients. A few months ago, we received FDA and CE mark approvals, making the *SAPIEN 3* platform the first and only TAVR device to receive US and European approvals for the asymptomatic indication. These approvals allow more patients to be treated earlier and avoid the clinical and economic pitfalls of waiting until symptoms present to be treated.

Our goal is for this to lead to the evolution of policy and guideline changes, some of which we've already seen with the updated European Society of Cardiology/European Association for Cardio-Thoracic Surgery [ESC/EACTS] guidelines for valvular heart disease, which establish a simplified care pathway for all severe aortic stenosis patients, regardless of symptoms. Together with the potential of a new US national coverage decision [NCD], this can help even more patients.

We're not just looking at severe disease. We're also focused on high-quality scientific evidence on moderate disease, which we think impacts even more patients than severe aortic stenosis. The enrollment and treatment on that wrapped up, two years ahead of schedule. You'll likely see data on that late next year.

Our evolution continues today. There are still structural heart patients with unmet needs, so we continue to innovate and find solutions. This was true 65 years ago, and it is true today. MTS