By Carolyn Gretton

Breaking New Ground: The Prix Galien Awards 2020

PRIX GALIEN

MEDSTARTUP

At the end of October, 2020, The Galien Foundation presented its 2020 Prix Galien Awards to six products in four categories: Best Pharmaceutical Agent; Best Biotechnology Product; Best Medical Technology; and Best Digital Health Product, a new category for 2020. Created in 1970, the Prix Galien is an international award recognizing innovating therapies that represent outstanding achievements in improving the human condition.

The Prix Galien is regarded globally as the equivalent of the Nobel Prize in biopharmaceutical and medical technology research.

We spoke to the winners of the 2020 Prix Galien about their reactions to the award and the development path traveled by these groundbreaking products.

BEST PHARMACEUTICAL AGENT: Pretomanid

MEL SPIGELMAN, M.D.
President and CEO
TB Alliance

Mel Spigelman, M.D., president and CEO of TB Alliance, called his company's Prix Galien award for pretomanid "a welcome surprise," given that it was TB Alliance's first year as a nominee, and the product was chosen out of a field of 26 strong nominees.

"I was proud to give an acceptance speech on behalf of our dedicated team at TB Alliance in which I had an opportunity to thank all our partners, donors and, above all, our clinical trial participants," Dr. Spigelman says. "They are the true heroes of this accomplishment. We cannot thank them enough for their contribution to ending TB."

Pretomanid was approved in 2019 as part of a three-drug, six-month, all-oral regimen for people with highly resistant forms of tuberculosis. The regimen, known as BPaL, includes the drugs bedaquiline, pretomanid, and linezolid.

TB Alliance is a nonprofit organization with a mandate to discover, develop, and deliver new treatments for TB. Pretomanid is only the third new medicine for drug-resistant TB to be approved in the past 40 years and the first to be developed and registered by a nonprofit organization.

Until recently, a diagnosis of extensively drug-resistant TB (XDR-TB) was regarded as a death sentence in many settings. During the first outbreak of XDR-TB in KwaZulu-Natal, South Africa in 2005, 52 of 53 people who contracted the disease died.

Results published in the March 5, 2020, issue of the New England Journal of Medicine show the BPaL regimen was able to successfully treat 90% of patients in a trial of 109 patients with XDR-TB in South Africa.

Dr. Spigelman notes that while TB is

among the world's deadliest infectious diseases, it is also a disease of poverty.

"This means that scant market incentives exist and far too few TB drugs have been developed while more than a million people are dying of TB each year," he says.

Dr. Spigelman says the TB Alliance was fortunate to in-license pretomanid early in its history and, with the support of its donors, was able to bring the compound from the early research stages through to approval.

"It has been approved as part of a combination regimen, which is a core principle of our drug development strategy — no one drug alone will be enough to end TB," Dr. Spigelman says.

As far as the future goes, Dr. Spigelman says TB Alliance is evaluating new combinations of anti-TB drugs that have the potential to be effective in treating every person with TB in a short, simple, safe, and effective manner.

"TB Alliance's vision, which is more urgent than ever in the wake of COVID-19, is an ultra-short and highly effective therapy that serves to lift immense burdens on patients and healthcare systems alike," he says. "To reach a point where a treatment course can be measured in days instead of months, we are exploring new approaches beyond developing regimens of newer and better antibiotics. This includes harnessing the power of the immune system to make effective regimens work even faster."

Dr. Spigelman says for the sake of the 10 million people who develop active TB each year, they cannot afford to stop being creative when it comes to fighting this disease.

BEST BIOTECHNOLOGY PRODUCT: Tegsedi

BRETT MONIA, PH.D.
CEO
Ionis Pharmaceuticals (and subsidiary Akcea Therapeutics)

Brett Monia, Ph.D., CEO of Ionis Pharmaceuticals and a founding scientist at Ionis who led the discovery and development of Tegsedi, says he was "thrilled and humbled" when he discovered Tegsedi had won the prestigious Prix Galien. "Upon receiving the award, I also reflected on the hard work, dedication and perseverance of so many people at Ionis as well as the patients, investigators, and caregivers, all of whom were instrumental in bringing this transformational medicine to patients," Dr. Monia says. "The journey was difficult with so many challenges along the way, so our team deserved this recognition."

Tegsedi is the first and only self-administered subcutaneous RNA-targeting therapy for polyneuropathy associated with hATTR amyloidosis.

This rare genetic condition causes abnormal formation of the human transthyretin (TTR) protein and a buildup of TTR amyloid deposits in tissues and organs throughout the body, including the peripheral nerves, heart, and intestinal tract. The accumulation of TTR amyloid deposits in these organs often leads to diseases such as intractable peripheral sensorimotor neuropathy and autonomic neuropathy.

Hereditary ATTR amyloidosis is a severe, progressive, and life-threatening disease, which causes a decline in quality of life and a significant negative impact on the activities of daily living. The disease often progresses rapidly and can lead to premature death, with the median survival being 4.7 years following diagnosis.

Dr. Monia says Tegsedi was the product initially of a collaboration he started with Merrill Benson, M.D., at Indiana University Medical School.

"Dr. Benson heard about the work we were doing to develop a platform called antisense to treat human diseases, and he reached out to me to discuss a potential collaboration," Dr. Monia says. "He introduced me to the field of TTR amyloidosis, and I introduced him to our platform drug discovery technology called antisense.

Ionis led the development and approval process to obtain marketing approval for Tegsedi, while Dr. Benson was the lead investigator. "It's a true 'bench-to-bedside' story with a very rewarding outcome," he says.

Tegsedi works by targeting RNA to reduce the production of TTR protein. The product's approval was based on data from the NEURO-TTR study, a 15-month international Phase III clinical trial in 172 patients with hATTR amyloidosis and symptoms of polyneuropathy.

According to study results, Tegsedi showed significant improvement compared with placebo in measures of neuropathy and quality of life.

The approval is also based on data from the NEURO-TTR Open Label Extension (OLE), an ongoing study for patients who completed the NEURO-TTR study that is designed to evaluate the long-term efficacy and safety of Tegsedi.

Looking to the future, Dr. Monia says Ionis is working on an additional treatment for patients with polyneuropathy of TTR amyloidosis that he expects to provide even greater benefit.

"This medicine, IONIS-TTR-LRx, is a ligand-conjugated antisense (LICA) medicine that is currently in the final stages of development that addresses all forms of TTR amyloidosis," he says. "We hope to bring IONIS-TTR-LRx to patients in the next few years as another option to treat this devastating disease."

2020 Galien Award Winners

Best Pharmaceutical Agent:
- TB Alliance's Pretomanid

Best Biotechnology Products:
- Akcea Therapeutics and Ionis Pharmaceuticals' Tegsedi
- Alnylam Pharmaceuticals' Onpattro (patisiran)
- Pfizer's Vyndaqel (tafamidis meglumine)

Best Medical Technology:
- Abbott's MitraClip Transcatheter Mitral Valve Repair System

Best Digital Health Product
- Pear Therapeutics' Somryst

BEST BIOTECHNOLOGY PRODUCT: Onpattro

JOHN MARAGANORE, PH.D.
CEO
Alnylam Pharmaceuticals

Onpattro is the first treatment to be approved by the FDA for polyneuropathy of hATTR amyloidosis in adults. John Maraganore, Ph.D., CEO of Alnylam Pharmaceuticals, says it was the result of almost two decades of determination to make this new class of medicines a reality for patients.

"There was an urgent need for effective new treatment options for hATTR amyloidosis that impact the underlying cause of the disease," he says.

The company was thrilled to receive the Prix Galien for Onpattro.

"Receiving the award also gave us a moment to reflect on the incredible patients, caregivers, scientists, healthcare professionals, and colleagues who all helped make this advancement possible," Dr. Maraganore continues.

Dr. Maraganore says the idea for Onpattro began with the Nobel Prize-winning science

of RNA interference, a natural cellular process of gene silencing that the company believes could revolutionize how many diseases are treated.

Hereditary ATTR amyloidosis is caused by mutations in the TTR gene, which is produced primarily in the liver. Earlier research showed RNAi therapeutics can target genes specifically expressed in the liver.

"Onpattro works to dramatically reduce TTR production by targeting the source, rather than the consequence, of the problem," Dr. Maraganore says.

Dr. Maraganore recalls that the 16-year journey to develop Onpattro was not without challenges. "Countless hours were spent in the lab to overcome some of the difficulties with delivering siRNAs into human cells in a stable way," he says. "All of this work led to a solution — encasing our siRNA within lipid molecules — creating a 'grease ball' that would enable us to deliver them to the liver and ferry siRNA molecules across the cell membrane. This became the basis of the proprietary formulation of Onpattro as a lipid nanoparticle (LNP) which allows for delivery to hepatocytes in the liver, the primary source of TTR production."

Onpattro is approved to treat polyneuropathy of hATTR amyloidosis in adults in more than 30 countries.

Alnylam is also conducting a Phase III study of Onpattro to treat the cardiomyopathy of ATTR amyloidosis, both the hereditary and wild types.

"Our efforts to develop new treatment options for those living with hATTR amyloidosis also continue with vutrisiran, a low-dose, once-quarterly, subcutaneously administered investigational therapeutic which uses our next-generation delivery platform known as ESC-GaLNAc," Dr. Maraganore says. "By contrast, Onpattro is delivered intravenously."

BEST BIOTECHNOLOGY PRODUCT: Vyndaqel

SENG CHENG, PH.D.
Chief Scientific Officer
Pfizer Rare Disease

Vyndaqel was approved by U.S. regulators in 2019 for the treatment of cardiomyopathy of wild-type or hereditary transthyretin-mediated amyloidosis (ATTR-CM) in adults to reduce cardiovascular mortality and cardiovascular-related hospitalization

Vyndaqel and its companion product Vyndamax are oral formulations of the first-in-class transthyretin stabilizer tafamidis and the first and only medicines approved by the FDA to treat ATTR-CM.

"We were incredibly excited to win this award, as it reflects Pfizer's dedication to create a meaningful difference in patients' lives," says Seng Cheng, Ph.D., chief scientific officer, Pfizer Rare Disease. "We are especially grateful to everyone who helped us achieve this milestone, including those involved in the development of these innovative medicines, the researchers and investigators who partnered with us, our rare diseases team, and, most importantly, the patients who participated in our clinical trial program."

Transthyretin amyloid cardiomyopathy is a rare, life-threatening disease characterized by the buildup of abnormal deposits of misfolded protein called amyloid in the heart.

About 100,000 people in the United States are believed to have ATTR-CM, and only 1% to 2% of those patients are diagnosed today. ATTR-CM patients have a median life expectancy of approximately two to three and a half years from diagnosis, depending on the subtype.

ATTR-CM is characterized by restrictive cardiomyopathy and progressive heart failure. Before Vyndaqel, the only available options to treat this type of cardiomyopathy were symptom management and, in rare cases, heart or heart and liver transplant.

The FDA approval was based on data from the pivotal Phase III Transthyretin Amyloidosis Cardiomyopathy Clinical Trial (ATTR-ACT), which showed Vyndaqel significantly reduced all-cause mortality and frequency of cardiovascular-related hospitalizations compared with placebo over a 30-month period.

"We look forward to continuing to make progress on our goal of delivering breakthroughs that change patients' lives," Dr. Cheng says. "Vyndaqel certainly embodies this goal and we are committed to helping to bring awareness to ATTR-CM and ensuring patients with this rare disease are able to receive treatment."

BEST MEDICAL TECHNOLOGY: MitraClip Transcatheter Mitral Valve Repair System

MICHAEL DALE
Senior VP
Abbott Structural Heart Business

Michael Dale, senior VP of Abbott's structural heart business, says everyone at Abbott was "incredibly honored" upon hearing that MitraClip had won a Prix Galien.

"While MitraClip is recognized as a transformative innovation today, the journey began more than 16 years ago, so this kind of recognition is especially poignant for our employees, scientists, and physician partners," Mr. Dale says. "For me personally, it is an honor and privilege to accept this award because I do so on behalf of Abbott and all those who have worked tirelessly over the years to make MitraClip the reality it is today for the millions of patients living with debilitating mitral regurgitation (MR), also known as leaky heart valve."

This is the second straight year an Abbott device has won the Prix Galien for Best Medical Technology, having won one for its FreeStyle Libre 14-day continuous glucose monitoring technology in 2019.

MitraClip is a small, clip-like device that repairs both primary and secondary MR without the need for open-heart surgery.

The safe, minimally invasive procedure restores proper functioning of the mitral valve and provides almost immediate symptom relief. MitraClip patients are generally discharged from the hospital within two days, allowing them to return to their regular lives much faster than open-heart surgery.

The device is approved in more than 75 countries spanning regions in Asia, Africa, Europe, the Americas, and Australia.

Mr. Dale says MitraClip was inspired by the "Alfieri edge-to-edge surgical procedure," a technique that still involved open-heart surgery but inspired others to think about how to replicate the edge-to-edge approach using a minimally invasive, transcatheter approach.

"It took time to perfect the transcatheter approach and prove its safety and efficacy benefits with objective evidence, but today, MitraClip is the standard of care for many patients with mitral regurgitation, the most common type of heart valve disease," he says. "Despite being one of the most common heart conditions, most MR was not treatable through the conventional surgical methods and until MitraClip arrived most sufferers of leaky heart valves had limited to no opportunities for treating their condition."

MitraClip is delivered through a vein in the leg up to the heart where it is then placed to grasp portions of the mitral valve leaflets and clips them together to prevent regurgitation or backward flow of blood into the heart safely and effectively.

According to Mr. Dale, what makes MitraClip special and a lesson for innovators in the treatment of cardiovascular disease has been its "profoundly positive" benefit versus risk profile.

"A primary consideration of whether an intervention is justified and appropriate is

the answer to the question, 'does the benefit of this treatment outweigh the risks?' The question is simple, but often, the answer can be ambiguous at best," he says. "MitraClip was unique from its beginning; the safety and predictability of the procedure was excellent, and the benefits have only grown and improved. Said another way, MitraClip honors every clinician's goal to 'first do no harm.'"

Since MitraClip was introduced in the United States in 2013, Abbott has continued to innovate and improve the platform to better meet the needs of cardiologists.

Now on the fourth generation of the device, MitraClip offers advanced steering and clipping capabilities and a greater range of clip sizes that allows physicians to customize the repair procedure to each patient's unique mitral valve anatomy.

"Today, this revolutionary technology has been used to treat more than 100,000 patients worldwide in more than 75 countries," Mr. Dale observes.

According to Mr. Dale, future plans include continuing to build on MitraClip's 16-plus year track record and potentially adding new technologies to the mix.

"There is a tremendous future advancing science in the structural heart space based on the integration of imaging and AI, which together, we believe will be enablers of treating even more patients with MitraClip as well as our other structural heart devices," Mr. Dale says. "We truly believe the treatment of cardiovascular disease is entering a renaissance based on the convergence of these new modalities with existing device technologies, and we fully intend to lead the way in applying these new capabilities."

BEST DIGITAL HEALTH PRODUCT: Somryst

COREY MCCANN, M.D., PH.D.
President and CEO
Pear Therapeutics

Corey McCann, M.D., Ph.D., president and CEO of Pear Therapeutics, says he felt "humbled and thankful" for Somryst to be awarded the Prix Galien.

"I was excited to share the news with all my colleagues at Pear whose many contributions led us to being recognized with the extraordinary honor of Best Digital Health Product," Dr. McCann says. "We are proud to provide patients with Somryst and continue forward in our efforts to make prescription digital therapeutics the standard of care across a range of diseases."

Somryst is the only FDA-authorized therapeutic that delivers cognitive behavioral therapy for insomnia (CBTi), the guideline recommended long-term, first-line treatment for chronic insomnia.

The nine-week prescription digital therapeutic (PDT) can be used on a mobile device, such as a smartphone or tablet.

CBTi has longer-lasting benefits than other treatment options, but the majority of insomnia sufferers do not have access to it and thus do not receive the recommended treatment. These factors create a significant unmet need for patients and higher costs for payers.

Dr. McCann says Pear developed Somryst to address this limitation by providing CBTi access digitally to treat the underlying factors of chronic insomnia and reduce barriers to treatment.

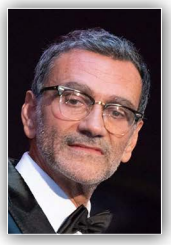
Somryst's therapeutic content consists of six cores that deliver multimodal CBTi treatment, including mechanisms of action of sleep restriction and consolidation, stimulus control, cognitive restructuring, sleep hygiene, and relapse prevention.

"Its content encourages engagement, facilitates active learning, and promotes behavioral change; its algorithms support tailored experience; and a clinician dashboard allows for patient monitoring to support treatment," Dr. McCann says.

According to Dr. McCann, Pear recently launched Somryst via an end-to-end virtual care experience combining virtual doctor visits via telemedicine provider with PearConnect, the industry's first patient service center for prescription digital therapeutics.

"With the first three FDA-authorized products, reSET, reSET-O, and Somryst, we continue in our efforts to make prescription digital therapeutics the standard of care across a range of diseases," he says.

The Prix Galien Awards



BRUNO COHEN
Chairman
The Galien Foundation

The Prix Galien Awards were created in 1970 and launched in the United States in 2007 and since then, the Galien Foundation has had the honor to reward excellence in scientific innovation to improve the state of human health. Regarded as the equivalent of the Nobel Prize in biopharmaceutical research, the Prix Galien USA Awards Committee evaluate and award innovations in the following categories: Best Biotechnology Product, Best Pharmaceutical Agent, Best Medical Technology and the newest category, Best Digital Health Product. Innovations in these categories have never been more crucial, as we've seen from a year unlike any this generation has witnessed.

The Galien Foundation Awards provide an opportunity to recognize these successes with perspective from a rich history of evaluating global achievements, paired with the renowned USA Committee's assessment of today's advances in order to encourage such triumphs for generations to come.

As 2020 celebrates 50 years of the Prix Galien process, this year's nominees showcased determination and passion for change to ensure a healthier future for generations to come. The foundation reached the highest number of applications ever received in spite of the very challenging environment due to the pandemic.

The Prix Galien USA Awards Committee was overwhelmed with excitement by the quality of submissions they received for each category and the impact these innovations have had for patients, starting from just ideas in a lab to FDA-approved products that improve human life.

We were particularly and pleasantly surprised with the positive response to the new Best Digital Health Product category, one which we'd now be remiss to not promote and evaluate exciting innovations for in future ceremonies.

The industry's commitment to innovation is at a record high given the current COVID-19 landscape. The pandemic has changed our daily lives and, right now, the whole world is watching the persistence and vigorous efforts it requires to develop a product and have it approved. Research teams have discovered multiple vaccines in less than a year, and it is inspiring to see how the biopharmaceutical industry wasted no time in finding a solution for individuals in great need around the globe.

It is an honor to not only witness these developments, but also to be reminded of the tireless passion these researchers and scientists have to create lifesaving innovations for millions of people.