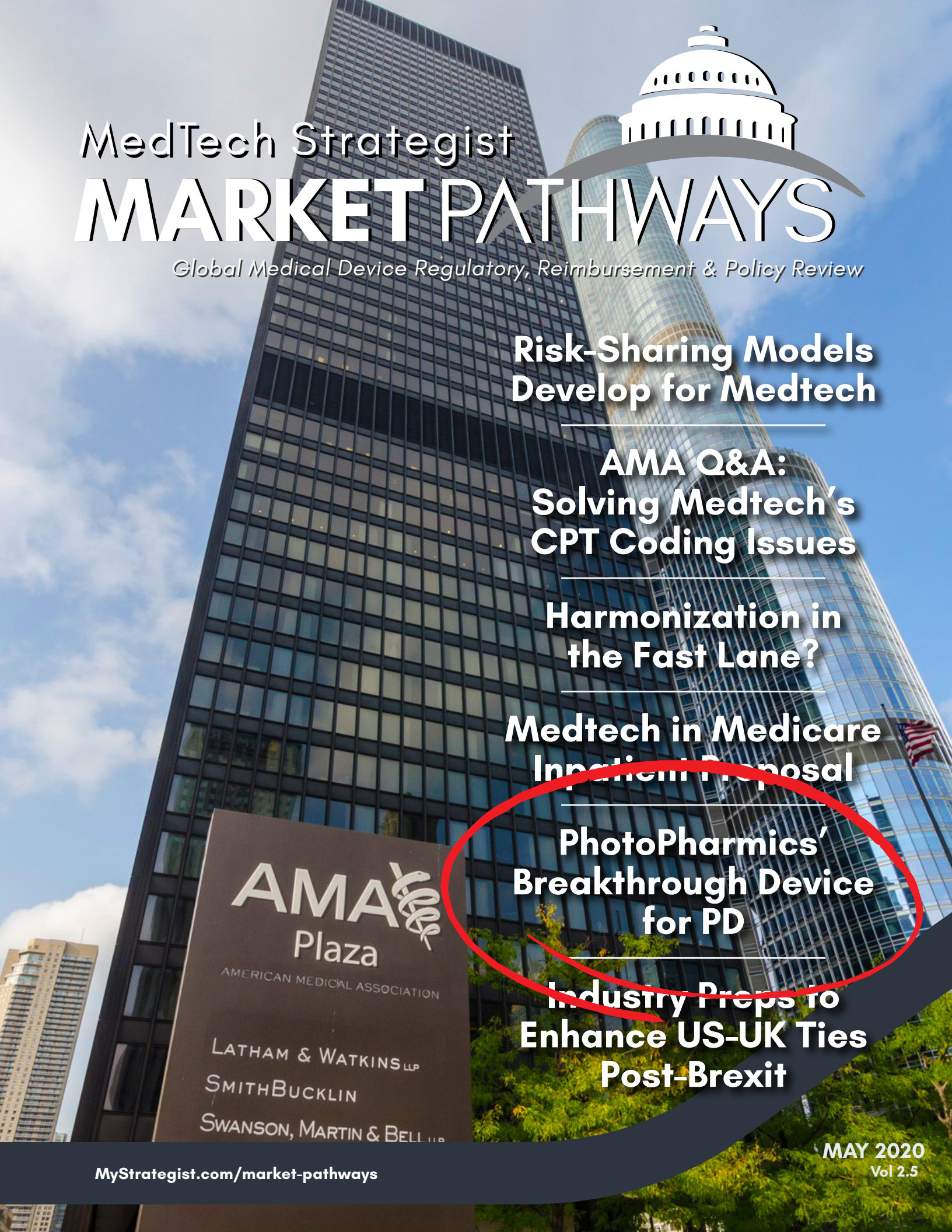

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STORIES WE'RE TRACKING

PhotoPharmics:
Shining a Light on Parkinson's Disease With a Breakthrough Device

The company is developing the first light-based, at-home device used as an add-on Parkinson's disease therapy to receive a 510(k) *de novo* classification and Breakthrough Device designation from FDA. Importantly in light of the COVID-19 pandemic, its upcoming Phase III trial will be remote, and then the next hurdle will be EU MDR.

>>Tracy Schaaf

PhotoPharmics Inc. is literally shining light on an increasingly prevalent neurodegenerative disease with no cure, and few treatment options: Parkinson's disease (PD). The company, founded in 2011 and headquartered near Salt Lake City, UT, is the first with a specialized, home-use phototherapy device to receive the FDA Breakthrough Device Designation, this April, after the firm submitted a *de novo* classification marketing application in 2018. The company has a Phase III trial scheduled to begin enrollment this August, following FDA's request for additional efficacy data after a Phase II study narrowly missed its primary endpoint. Parallel to this, it is pursuing a European market strategy on the go-to-market version of its device, *Celeste*, and working through the challenging MDR certification and CE mark processes.

KENT SAVAGE

BRETT WALKER

Market Pathways spoke with PhotoPharmics' CEO, Kent Savage, and Senior Vice President, Brett Walker, about the company's regulatory and reimbursement journey to date, and its fortunate position during the current COVID-19 crisis as a device designed from the beginning to be clinically tested remotely and used by the patient in their home. The company's founders have more than 30 years of experience in the phototherapy field, having previously developed specialized light solutions that are now widely used to regulate circadian rhythms in treating seasonal affective disorder, sleep disorders, anxiety, and depression for Apollo Light Systems, which was led by Savage and acquired by Philips-Respironics in 2007. "We've been in development for many years and are eager to get a solution into the hands of people

with Parkinson's, so that they can return to doing the things that they love," says Savage.

PhotoPharmics believes that the main principle behind its clinical-stage *Celeste* technology is regulation of the body's natural circadian rhythm, that responds primarily to light and darkness in the environment (the device builds on the company's innovative *Spectramax* technology that has been used in previous human research). In PD, the circadian system is dysregulated, which impacts the motor and non-motor symptoms of the disease, ranging from tremor and stiffness to fatigue and sleep, gastrointestinal, cognition, mood, and other disorders. PhotoPharmics' home-use, non-invasive light therapy device uses specialized phototherapy, a combination of light intensities and bandwidths intended to target the photoreceptors in the eye, creating a therapeutic effect by improving the circadian rhythm and helping to ease disease symptoms.

PD is the second-most-common neurodegenerative disease after Alzheimer's, affecting an estimated 7 to 10 million people worldwide, including more than one million in the US. Nearly 60,000 Americans are newly diagnosed each year, a number which is expected to double within the next 20 years. Most current treatments for PD primarily address the disease's motor symptoms, but very few options exist for the debilitating non-motor symptoms, which can often appear years before the classic markers of PD. As Parkinson's progresses, these non-motor issues become even more pronounced and are often the primary determining factors for quality of life and eventual institutionalization.

PhotoPharmics' phototherapy technology has been shown in clinical trials to improve the significant non-motor symptoms of PD and improve quality of life. Research participants found the device, about the size of a laptop computer, to be safe and convenient to use while watching TV, reading, using a smartphone, or other seated activities, with daily therapy times of 30 to 60 minutes (see *Figure 1*). Those who added specialized phototherapy to their existing drug regimen experienced no major device-related side-effects or negative interactions with their current PD medications.

"In our Phase II trial, the most effect we saw was in the non-motor function areas. It's a crying need that often goes unnoticed or undertreated in Parkinson's patients," says Savage. "In our early studies, we've seen people return to work, and get back to some of the things they enjoy in terms of social activities and other things," adds Walker.

The technology also has the potential to provide meaningful real-time telehealth data, via a smartphone app that the company is developing. "This could provide new possibilities for patient-reported outcomes, edutainment, and other digital interactions. Patients could be truly engaged in their home-based therapy," says Walker. A smartphone app could also help reinforce the telemedicine relationship and track patient adherence.

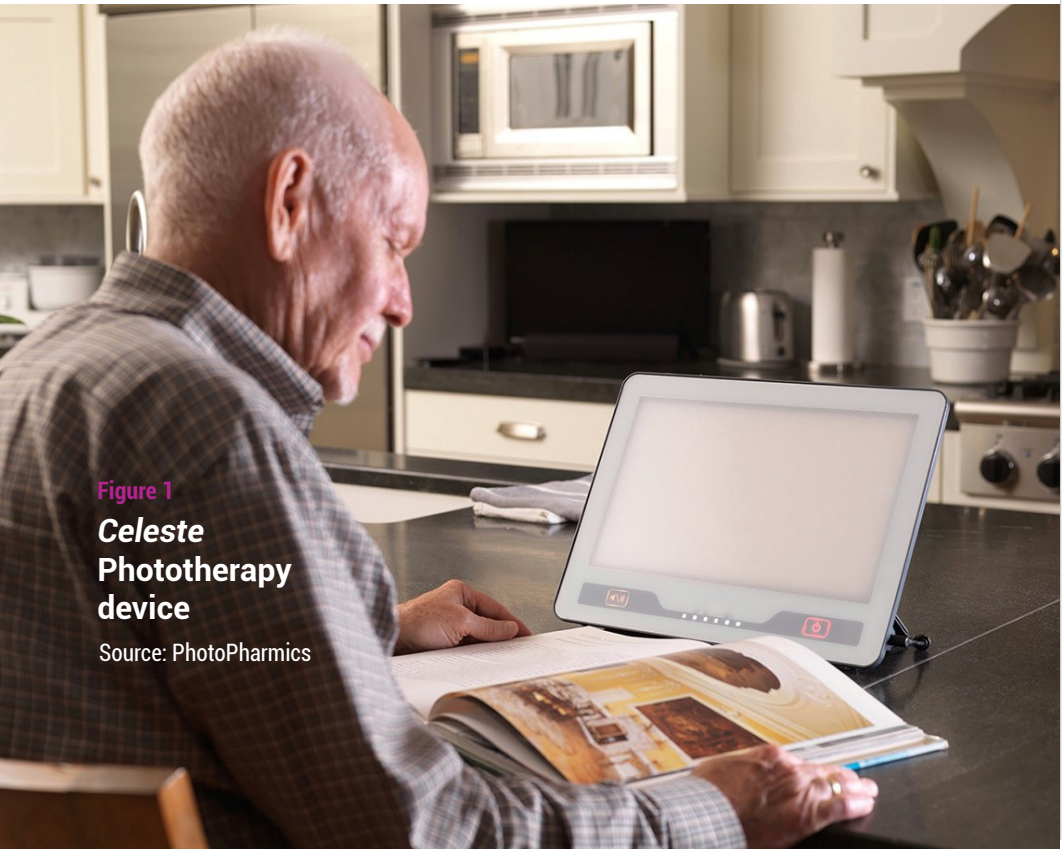

Figure 1
***Celeste* Phototherapy device**
Source: PhotoPharmics

From *De Novo* to Breakthrough

The company is pursuing the US market via the *de novo* pathway, and FDA accepted its *de novo* submission for review in 2018. The *de novo* route is available to low- to moderate-risk devices where no predicate has been cleared by the FDA. In February 2018, the company completed a first-of-its-kind, multinational, double-blind, randomized clinical trial of its pivotal *Spectramax* medical device.

The multicenter trial involved 92 patients and established the safety and efficacy of *Spectramax* phototherapy for motor and non-motor symptoms in Parkinson's disease. In the trial, patients ages 45 or older, all on stable dopaminergic therapy, were treated with either its

light therapy device or a placebo light for one hour each evening for six months. The trial was conducted at Massachusetts General Hospital in Boston, Vrije Universiteit Medical Center in Amsterdam, The Netherlands, and Aspen Clinical Research in Salt Lake City. Results, released in late 2018 and based on scores reported by both patients and doctors, showed an easing in disease severity, lesser non-motor symptoms, and improved quality of life among those given the light therapy.

The study narrowly missed statistical significance in its primary efficacy endpoint (*p* value of .07), although the technology demonstrated clinically meaningful improvement in quality of life and combined motor and non-motor function in patients. "We saw really large clinical improvement in the Parkinson's patients as compared to placebo, much larger than what you see in most new interventions," says Savage.

Savage notes that PhotoPharmics' original plan was to gain CE mark certification in Europe, and the company sized its clinical trial for that market. "We started out that way, and then part way through the trial we made the decision to add more patients and go to FDA. We actually did not have a pre-submission meeting before we kicked off our trial because it wasn't originally targeted for the FDA."

The company proceeded to submit a *de novo* application with the FDA, and the agency came back with a request for additional efficacy data. In response, this February, PhotoPharmics announced plans for a pivotal Phase III trial with the University of Rochester's Center for Health + Technology (CHeT) to assess the efficacy of its latest-generation *Celeste* device. The company anticipates enrolling up to 200 patients, beginning in August, in what will likely be the largest trial of its kind.

Importantly, in light of the significant disruption that the COVID-19 pandemic has caused to clinical study integrity and protocols, the company's upcoming trial will be held remotely in the patient's home environment. "CHeT has been doing remote trials for 10 years and they're really the leaders in the US for remote neurological trials, in particular. They've done a lot in Parkinson's disease and we really have a great team assembled to conduct our Phase III work," says Savage. "We planned our at-home protocol more than nine months ago, with the idea that it allows access to patients all throughout the US. Rural patients for example, who don't always have access to best care or to new clinical innovation. And then just the burden on people with Parkinson's disease to do an assessment at a Center of Excellence for example, it's often a five-hour ordeal for them. What better place to assess someone with Parkinson's than in their own home," he says. (*See recent FDA guidance around the conduct of medical product clinical trials during the COVID-19 public health emergency; also see "COVID-19 Crisis: Accelerating Transformation in Medical Device Research,"* Market Pathways, *March 25, 2020.*)

> *"We planned our at-home protocol more than nine months ago, with the idea that it allows access to patients all throughout the US."* —*Kent Savage*

Following this announcement, in late April, PhotoPharmics received word of its Breakthrough Device designation from FDA. "Our device is the first specialized phototherapy device ever to achieve this status," says Savage. Although the designation was just announced, the company has already seen a quick response from FDA. "They've assigned us some additional staff, which will be helpful," says Savage. "Also, they prioritize our interactions. We're turning in a supplement to our pre-submission meeting ahead of the clinical trial. Sometimes that takes 90 days to process, but we imagine that that will be a lot faster, and it will allow us to kick off our trial sooner."

Collaborative feedback from the agency has also been important. "I would point to the positive contributions the FDA made in shaping our own thinking that, we believe, will eventually lead us down a more successful path with the agency," adds Walker.

The company is also raising a B round to finance its pivotal study. "From an investor perspective, if they are in life sciences and want to be involved with new innovations that make a big difference for people, this is a nice investment opportunity because our trial can move forward while other trials are unfortunately shut down because of COVID-19," says Savage. In addition, the company recently submitted a grant application to the Michael J. Fox Foundation and will work with them on recruitment.

Observations and Advice

Savage offers advice to others that might be looking at a Breakthrough Device pathway, including the value of the pre-submission process. "The pre-sub process is very important, and I would advise taking advantage of those meetings. We found good access to the FDA through the pre-subs and good collaborative feedback," says Savage.

The company also emphasizes the positive impact that key opinion leaders have had along the way. "A piece of advice for other small companies, our work with key opinion leaders has been critical. As they've looked at our data

and we've met with them, they've helped guide even the marketing efforts by identifying what the real needs are with our product," says Savage.

Additionally, Savage notes that having good support from its regulatory attorneys has been very important to the company's overall strategy. And, for more mature companies, he advises having quality processes and systems in place well ahead of time.

Next Hurdles: Reimbursement and MDR

In terms of a reimbursement strategy in the US, the company has had preliminary discussions with ex-CMS staff, regarding offering its device positioned as a therapy, and not just a purchased device. "Typically, devices used in the home are considered durable medical equipment. Because of this, securing reimbursement for a device-delivered therapy is high on our list of priorities," says Walker. "An ideal goal would be to be reimbursed much like a pharmaceutical is today, with some monthly reimbursement. There's not a refill here, but it's the equivalent, and that's how you continue to benefit from the therapy," says Walker. "We think CMS will be warm to this. This is breaking some new ground obviously with the FDA, and CMS should view it in the same light."

Some older, less-favorable CPT codes apply to phototherapy technology, but PhotoPharmics is assessing whether new codes would be needed for its *de novo* device. Also, as the device has been designated as a Breakthrough Device, this should help satisfy CMS' need for understanding whether the technology is new or not, in terms of categorization and reimbursement. "We've got some work to do there, including a cost benefit analysis, but we're not daunted by it," says Walker. "We're hoping that CMS actually does more in this regard to recognize Breakthrough devices as something that needs to get to market immediately." (Under the 2020 Inpatient Prospective Payment System rule, CMS finalized an alternative New Technology Add-On Payment eligibility pathway for transformative new devices.)

The company is also now dealing with the implications of the European Union Medical Device Regulation (MDR). It plans to gain CE mark for its go-to-market model that will require MDR certifications (it had CE mark clearance on the early, clinical trial version of its device, *Spectramax*). "We are working in that direction, we have contracts with a notified body already," says Savage. "We look at that as potentially a way of getting something into the hands of people with Parkinson's in an independent, parallel timeline to what we can do in the US," adds Walker. "MDR's a new thing, Brexit still settling. The best data we have says that we'll still have one certification with a unified outreach to all of Europe."