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MARKET TRACK

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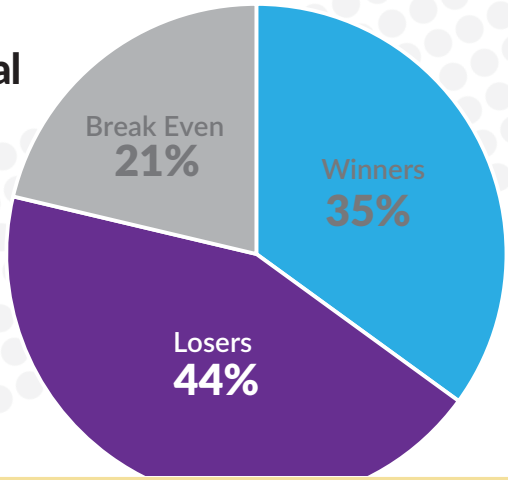
The Fate of Medical Device Exits



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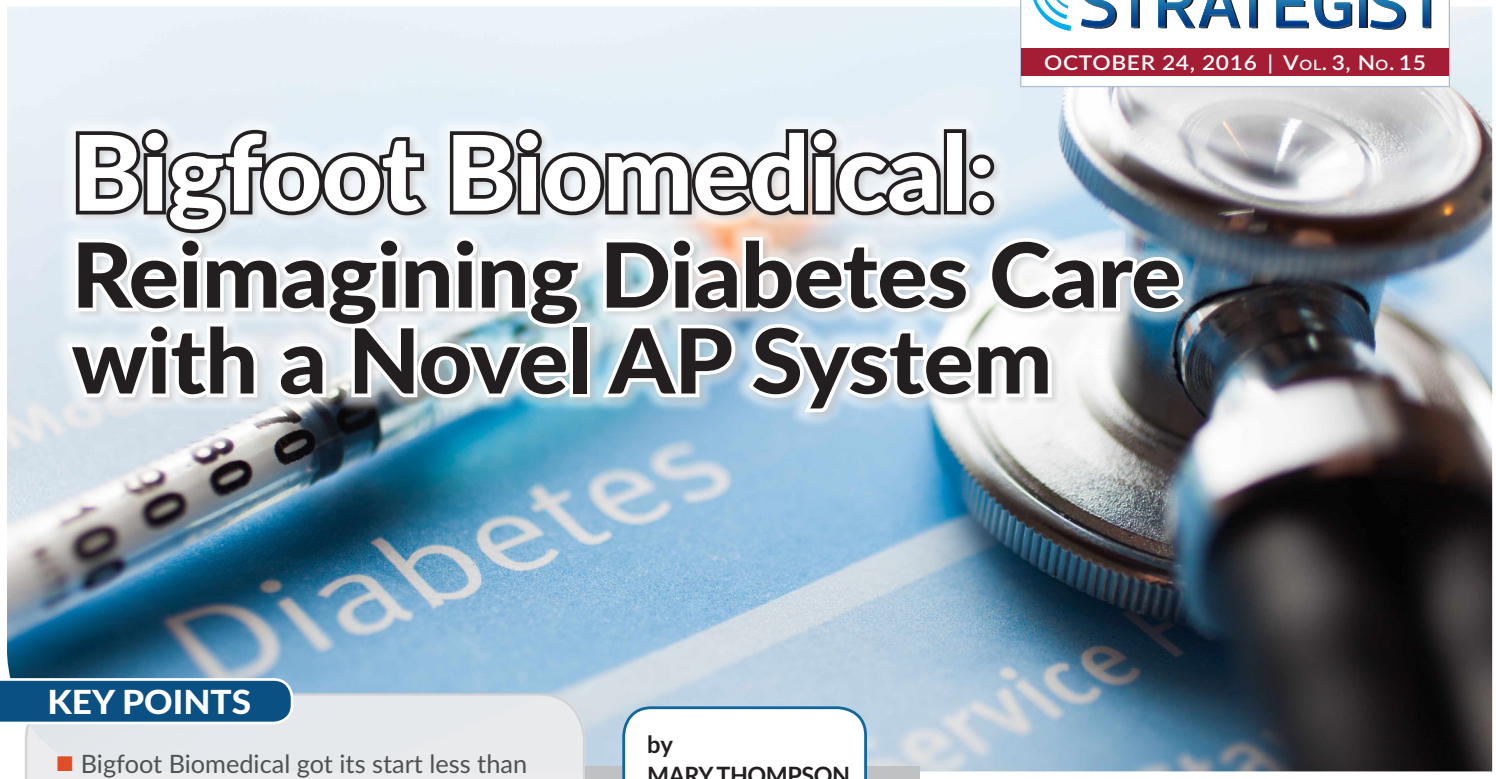

Bigfoot Biomedical: Reimagining Diabetes Care with a Novel AP System

KEY POINTS

- Bigfoot Biomedical got its start less than two years ago, but the young company has already made considerable progress in its quest to develop a best-in-class automated insulin delivery system that is truly patient-, physician-, and payor-friendly.
- The company's four founders all have a close connection to the type 1 diabetes patient community, and two were leading players in the "Do-It-Yourself AP System" and "we are not waiting" movements that helped jump-start the current trend toward more connected, technology-enabled diabetes care.
- Bigfoot's current *smartloop* automated insulin delivery system combines the company's proprietary algorithms with a network of secure, Bluetooth-enabled wearable devices, including a patient-friendly pump platform the firm obtained when it acquired the assets of Asante Solutions last year. The entire system is viewed and operated via the user's smart phone.
- The firm is also pursuing a novel, more cost-effective business model and plans to provide its system and all the necessary supplies for one monthly service fee.
- The *smartloop* system entered its first IDE-approved feasibility trial this past summer and a phased pivotal trial could begin in 2017.

by
MARY THOMPSON

With FDA's earlier-than-expected approval last month of **Medtronic plc**'s *670G* hybrid (treat-to-range) closed-loop insulin delivery system, the artificial pancreas (AP) concept—not so long ago, just a futuristic idea—has taken a huge step forward (*see Sidebar, "Medtronic and Abbott Score Important FDA Approvals in Diabetes Device Space"*).

But Medtronic is not the only AP game in town. There are now a number of competitors, both large and small, pursuing this opportunity. One young company that hopes to make a big difference in this space is **Bigfoot Biomedical**.

Bigfoot has been generating a great deal of interest within the diabetes community of late, and not only because of its unusual name. The company brings together leading players in the "Do-It-Yourself AP System" and "we are not waiting" movements—diabetes community-led efforts that helped jump-start the current trend toward more connected, technology-enabled diabetes care. Its aim is to offer a best-in-class AP that is secure, highly connected, highly automated, and truly patient-, physician-, and payor-friendly. Although it's still early days for Bigfoot, the company has been progressing rapidly, with clinical trials already underway and high hopes for the future.

For Bigfoot, It's Personal

Unlike many of the large diabetes device players, for the folks at Bigfoot Biomedical, the quest to develop and commercialize an automated insulin delivery system is personal. Many of the principals at Bigfoot have close family members with type 1 diabetes (T1D), which gives them a unique perspective on the challenges and unmet needs associated with this disease. As a result, the firm's overall goal has always been to simplify the diabetes disease burden. In fact, says CEO Jeffrey Brewer, the company aims to help people "reimagine the entire experience of living with diabetes."

Bigfoot Biomedical got its name in February 2015, but its roots go back much further. Brewer, who co-founded the company, began his journey into the world of diabetes care when his son was diagnosed with T1D in 2002 at the age of seven. Brewer had spent his working career in the technology world and founded several successful Internet companies. In 2002, he was about to turn his life toward philanthropy when his son's diagnosis dramatically changed his path. At that time, he says, he knew next to nothing about type 1 diabetes. But he quickly learned about the importance of insulin and the delicate balance that proper insulin dosing requires—too much can lead to unconsciousness or even death and too little leads to devastating diabetes complications down the road.

He also quickly gained first-hand experience about the daily disease-management burden that comes with a diabetes diagnosis. "People with T1D have to make a lot of decisions," he says, "based on their blood glucose level, what food they consume, how much exercise they do, and other variables." And, when they are seven years old, "those types of calculations and decisions are the responsibility of the parents." Among other things, that meant getting up two or three times every night to check his son's blood glucose levels, which he notes, was tough on everybody.

Coming from a high-tech background, Brewer naturally began looking for available technology tools to help his family manage this burden—and he was surprised to find that there really were none. All he was given, he recalls, was a piece of paper with a hand-drawn sliding scale showing how much insulin to give his son based on his blood sugar readings. "I was just appalled," he says, "because I thought (even in 2002), we can land 747s on autopilot and we have missiles that can go around the world and strike within a meter, and this is the best we have for a very dangerous drug [insulin] that my son is now dependent upon."

Brewer began attending medical conferences, asking questions of medical device companies, academic researchers, and government agencies. In the process, he learned about insulin pumps and continuous glucose monitors (CGMs), and about the early work being done to link the two into an artificial pancreas by creating a feedback loop between the pump and CGM.

"I started asking the companies, so how is this [work] going? When can I buy this for my son?" he recalls. But they were less than encouraging and it wasn't because of the underlying technologies—"it was more about the business of developing and delivering these devices."

There were, in fact, a number of market-limiting factors in play at the time. For one thing, the regulatory pathway for an AP—which is essentially an automated insulin delivery system—was murky. FDA had no clear guidance on how to test the safety and efficacy of such a device, and that added a lot of risk to the task for the companies involved. In addition, the device companies he spoke with also were worried about adoption. Doctors weren't keen on prescribing insulin pumps at the time, and insurance companies didn't want to pay for them, so naturally they weren't eager to bet on a combination pump and CGM system. Bottom line, notes Brewer: "there were a lot of systemic challenges in the system that really had nothing to do with the technologies themselves."

To help move the AP solution forward, Brewer worked with the Juvenile Diabetes Research Foundation (JDRF) to establish and head-up JDRF's Artificial Pancreas Project. (Founded in 2005, that project is now partnered with more than two dozen entities on AP research worldwide—*see "Technologies to Watch in 2016: New Entrants to Watch in the Artificial Pancreas Space,"* The MedTech Strategist, *February 9, 2016.*) The AP Project, he notes, was launched to help fund research, advocate for regulatory clarity in the AP field, and gather healthcare economics data demonstrating the cost benefits of technologies such as CGMs.

JDRF's AP Project supplied grants to help fund technology development work at facilities around the world, including many of the major device companies working in this field. "We raised more than $100 million over ten years," Brewer says, "and invested directly with device companies like Medtronic, **Becton Dickinson**, **Roche**, and others to provide financial support in order to de-risk some of their development efforts and move the ball forward." But, he continues, "We had less success than we ever expected. And still today, we find that technology is fundamentally not being applied to this problem in a way that would really change lives."

Brewer was a volunteer, donor, and board member at JDRF until 2011, when he was tapped as JDRF's new CEO, a position he held until 2014. By that time, he was looking for another way to move AP development in the direction he believed it needed to go. "At a certain point, I realized that the kind of innovation that's necessary to solve this problem would have to be robust and simple—more like the consumer devices we're used to in the rest of our lives."

He also was keenly aware that tech-savvy diabetes patients (and parents), tired of waiting for industry-led solutions, had started to take matters into their own hands and had made some impressive progress. They discovered how to "hack into" existing CGMs so they could remotely monitor the data, and they were even developing their own feedback loop algorithms to connect CGMs with insulin pumps, with the aim of constructing their own "home-made" AP systems. To date, more than 100 people have created their own AP systems using do-it-yourself feedback-loop algorithms developed and shared through what is now called the OpenAPS project, which provides free, open-source AP tools to anyone who wants to use them, including patients, researchers, and commercial manufacturers.

In 2014, the undisputed leader of the AP do-it-yourself movement was Bryan Mazlish, who was the first to develop his own home-made closed-loop insulin delivery system. Like Brewer, Mazlish's motivation came from personal experience—his son was diagnosed with T1D at age five and his wife, a Harvard-trained pediatrician, also had the disease.

Mazlish also was walking a very different path when his son was first diagnosed in 2011. He had carved out a successful career in quantitative finance, managing one of the world's largest securities trading institutions and then founding a fully automated stock trading company. He was able to repurpose his expertise in automated stock trading algorithms for use in the diabetes field, creating algorithms that predicted blood glucose trends based on CGM data as well adaptive insulin delivery algorithms capable of automating insulin delivery. He also developed a companion mobile app that allowed him and his wife to remotely monitor his son's CGM readings and alert them if his levels got too high or low (relieving them of the nightly glucose-check burden).

Mazlish's wife and son have been successfully using his proof-of-concept AP system since 2013, but when he tried to make his work available to device companies so that others could benefit, he was rebuffed. Brewer, who had met Mazlish through his work at JDRF, offered to provide introductions to the big device companies working in this field, certain they would jump on the opportunity to develop and commercialize this first-of-its-kind technology. But, amazingly, he recalls, there was no interest on their part.

In fact, notes Brewer, Mazlish "literally wanted to give away the technology and come to work for them for free" and they still weren't interested, in large part, he says, because Mazlish's highly integrated, connected solution didn't fit with their existing business and technology models. With the exception of Medtronic, insulin pump companies at the time "weren't really interested in getting into the AP business," explains Brewer, "because it would require them to think in a very different way about a combined offering that minimizes the value of the pump or sensor, but actually maximizes the value of the integrated whole—which is as much about software and connectivity as it is about the individual device components." (Of course, the field has progressed much further since then, and today, many of these same companies are working to create their own AP systems.)

"I tried for four years and spent $35 million trying to [get the big device companies to develop this technology]," Brewer says, and none of that came to fruition." Eventually, Brewer told Mazlish, "This isn't going to happen with the established players," and the two began to make plans of their own.

Bigfoot is Born

In 2014, they co-founded SmartLoop Labs to develop and commercialize their vision for an AP, with Brewer as president and CEO and Mazlish as chief technology officer. By then, Mazlish was something of a legend in the T1D community. Although he had carefully protected his anonymity, fearing a deluge of inquiries if his name got out, there were widespread rumors about his AP work and his identity. However, he was still such an enigma, when *Wired Magazine* got wind of his efforts and published an article in December 2014 on the do-it-yourself AP movement, they dubbed him "Bigfoot," after the legendary creature of urban myth. The moniker stuck, and when the time came for Brewer and Mazlish to give their new company a more permanent name, Bigfoot came to the top of the list. In February 2015, they changed the company's name to Bigfoot Biomedical, in part to acknowledge Mazlish's accomplishments, but also says Brewer, "to show we were different."

Brewer and Mazlish were joined by Lane Desborough, who came on board as chief engineer, and Jon Brilliant as CFO, both of whom also have children with T1D. Like Brewer and Mazlish, Desborough has a son with the disease. He also has 20 years of cumulative engineering experience at large companies, including GE and Honeywell, where he developed computer-based systems for controlling and remotely monitoring oil refineries and chemical plants around the world. In 2010, the year after his son was diagnosed, Desborough joined Medtronic's diabetes unit, eventually becoming chief engineer of Medtronic's insulin delivery/closed-loop business. In addition to his corporate experience, Desborough is also a co-creator of Nightscout, a free, open-source system that gives people with diabetes the tools they need to remotely share CGM data, and he helped found the influential T1D community-led "we are not waiting" movement, coining the phrase in 2013.

The net result is a company that brings something unique to the table: a remarkable depth of knowledge and technical know-how combined with the personal motivation and direct patient experience necessary to really make a differ-

ence in this space. In fact, about 40% of the firm's 40 employees have a direct connection to T1D, says Brewer.

Expertise and motivation are essential, of course, but a little luck is always good to have, too. And, in May 2015, Bigfoot Biomedical was fortunate enough to be in the right place at the right time when the assets of insulin pump maker Asante Solutions were put up for sale. Asante had developed the *Snap* insulin pump, which many patients had come to value for its convenience. *Snap* was the first insulin pump that used a prefilled insulin cartridge (made by **Eli Lilly**), which freed patients from having to manually fill the cartridge with insulin from a vial—a complex, time-consuming process.

However, notes Brewer, other aspects of the *Snap* pump kept it from making significant gains in the marketplace. For one thing, the pump was complicated for physicians to configure, he says, because it used "a very antiquated interface and wasn't a connected device." Moreover, payors saw the device as just another insulin pump, he says. As a result, the company was never able to differentiate itself from the big players in the market. After investing about $150 million in the *Snap* pump and bringing in about 1,000 users, Asante essentially ran out of money and was forced to discontinue operations.

At the time, Bigfoot's development team was considering its options with regards to system hardware and thought the Asante technology would provide a good starting platform. When Asante's assets went up for auction, Brewer knew he needed to act fast and decisively if the small company was to have any chance of beating out larger firms that might be interested. "We made an exploding offer to the people who were in charge of the assets," he explains, telling them "we'll write you a $5 million check and transfer the money overnight. But it's a one-day deal."

It was clearly a gutsy move, and Brewer had no idea if it would work, because "we knew this [technology] was worth a lot more to Medtronic and J&J." In fact, he continues, "in the days after we pulled off this coup, those companies started calling and telling us we could have flipped it for four times as much the next week."

But Bigfoot had other plans. Notes Brewer, "it was an amazing opportunity for us because we got a great insulin pump that was easy for consumers to use, and we got it for an amazing price."

In addition to the pump technology assets, Bigfoot also got all of Asante's operational infrastructure—including an FDA-validated manufacturing facility that Asante had recently spent $2 million to update. Bigfoot quickly moved its base of operations from New York City to Asante's former headquarters in Milpitas, CA, in the Silicon Valley, and began thinking about how to integrate its technology platform.

The company also was rethinking its timelines to market entry. The acquisition had the potential to "dramatically accelerate" Bigfoot's time-to-market, Brewer noted at the time, and the reasons for that are multifactorial.

In fact, he says, the Asante acquisition was the perfect opportunity for Bigfoot for two reasons. First, Asante's pump was the "easiest, most consumer-friendly" insulin pump on the market, Brewer notes. It doesn't require any training to teach people how to load the cartridge, which makes it easier and better for patients, and better for Bigfoot, he says, which doesn't have to pay patient training costs. But beyond that, the other compelling draw, says Brewer, was the particular architecture of the Asante pump, which had a durable controller and a disposable pumping mechanism. "The interface between those elements allowed us to use the disposable component—the insulin pumping mechanism—without making any changes. We only changed the controller mechanism."

> ***"At a certain point, I realized that the kind of innovation that's necessary to solve this problem would have to be robust and simple—more like the consumer devices we're used to in the rest of our lives."***
>
> ***—Jeffrey Brewer***

Since Asante's pump was already FDA-approved, and Bigfoot's changes didn't affect the actual pumping mechanism, that set the company up for a much faster and easier integration timeline. "This gave us an opportunity," explains Brewer, "to do a quick hardware development process whereby we replaced the controller with an 'Internet of Things' device." That device provides the automation algorithms, a crypto chip that sets a secure communications protocol with the other devices (the CGM, blood glucose meter, and smart phone), and basically serves as the hub on the body for all of the data transfer. "[All of] that we were able to do in eight months," he notes.

Bigfoot also inked several product development and supply agreements, including one in June 2015 with CGM market leader **DexCom Inc**., as well as supply agreements with **Agamatrix**, which makes a Bluetooth-connected blood glucose meter, and with **Unomedical** for its infusion set.

The company's integrated system, called the *smartloop* automated insulin delivery system, entered its first IDE-approved feasibility trial this past summer, and Brewer says the plan is to begin a phased pivotal trial around the second

quarter of 2017. Once that is complete, Bigfoot will file for FDA PMA approval, which he says could occur by the end of 2017 or early 2018.

The Goal: Smart, Secure, and Connected

The *smartloop* system currently being trialed utilizes a DexCom *G-5* CGM, widely regarded as the most accurate CGM currently on the market (*see Figure 1).* (*See also "DexCom Sets High Bar in Growing CGM Space," and "Taking Stock of CGM's Future: A Conversation with DexCom CEO Kevin Sayer,"* The MedTech Strategist, *August 24, 2016*.) Brewer says Bigfoot has worked very collaboratively with DexCom and the plan is to launch in the US with a DexCom sensor. However, he also stresses that the company has "built a modular system that provides opportunities to use different sensors that are approved for use in different environments." For example, he explains, DexCom's CGM is not currently available in China, so the firm may seek another sensor partner for the China market. "It's important that we have some flexibility for commercial and market reasons."

Unique Aspects of Bigfoot Biomedical's *smartloop* AP System

- **Viewed and operated via the user's smart phone**
- **Simple infusion pump tightly integrated with the CGM**
- **Secure, wireless on-body network of wearable devices**
- **Proprietary algorithms for closed-loop automation**
- **Cloud-based therapy personalization and remote monitoring**
- **New business model: single-prescription, reimbursed as a service for a monthly fee**

Source: Bigfoot Biomedical

But modularity is only one aspect of the integrated, connected system Bigfoot has envisioned. The aim in a nutshell, says Brewer, is to provide "a smart, secure, connected system that is simple for the primary care provider to prescribe so the bulk of people affected by this disease can get it."

What's different about Bigfoot, he explains, is the company is designing a set of devices and software "made to play in the modern world." And that means that a smart phone and its connectivity to the Internet will be an essential element. Other AP systems are so complex, he continues, they require endocrinologists to configure them and interpret the data. But there aren't enough endocrinologists today to absorb this burden, and there's little incentive because managing these devices is a financial burden for their practices, he says.

Bigfoot's big difference, says Brewer, is a system that can configure itself. All of the data passively captured via Bluetooth by the *smartloop* system (from the CGM and other sources), automatically goes to the smart phone and into the Cloud, he explains, and every day, the system reconfigures itself, in very small increments, based on that data. Thus, if a patient decides to go on a diet, or works late at night, gets sick, or runs a marathon—whatever life changes they have—the system detects that (by continuously monitoring glucose levels and trends), and automatically reconfigures the insulin dosage to take that change into account. "So this takes all of that off the table for the doctor and the patient," he explains, and optimizes the system around each patient's individual physiology and their particular habits, which is something even the most highly trained physicians can't do on their own. "We're just doing what the doctors would do if they had perfect information and all day long to do it." (Medtronic's recently FDA-approved *670G* AP also has adaptive learning capabilities. But Bigfoot says its algorithms will auto-configure the *smartloop* system for the patient from the beginning, simplifying training and clinician onboarding and expanding the clinical environments in which it can be prescribed and supported.)

Bigfoot's solution could be described as machine learning linked to the Internet of Things. Patients still need to alert the system when they are going to consume carbs and provide a general estimate of their carb intake, and no AP can eliminate mealtime bolus insulin yet because current insulin formulations take time to work when administered subcutaneously. But, other than that, says Brewer, "the system works in the background and is constantly doing projections based on the data." If the user is trending low, it will automatically lower the basal insulin delivery rate, and if they are trending high, it increases the rate. And, if the system predicts that it won't be able to fix the problem by making these adjustments, it alerts the user and tells them what they need to do. For instance, it may say "within an hour you're going to be out of acceptable range, so now you need to consume 15 grams of carbs—have a glass of orange juice." That may seem futuristic, but in fact it is easy to do, says Brewer, and relies on technologies that already exist—but it's "not being done by anybody [else today]."

"It's machine learning, and it's all done passively," says Brewer, who points out that "this is Bigfoot's real innovation." You can't rely on people to do this, he continues. "People get tired of this disease—there's only so much that they're willing to give to it on a daily basis. So you have to do as many things for them as you can." Even if a patient's infusion set fails because it's kinked or improperly inserted, the system can detect that, he says. That's a common problem, but today, people typically don't figure that out until they see a succession of high blood sugar readings, which can ultimately put them in the emergency room if it's not corrected. But the Bigfoot system "can actually detect that a person's not getting insulin within 30 minutes, just by looking at the data," says Brewer. At that point, the patient would be notified to check their infusion set and replace it.

"That kind of trouble shooting can be embedded into the logic of the app," he says. "We actually have detection algorithms that will flag things that don't make sense" and then tell the patient how to take corrective action.

The system will do the same for parents or other caregivers who are monitoring the data coming from a person with T1D. "Our system is smarter [than what's out there today]," Brewer asserts, because "it will notify people with exceptions." Thus, parents monitoring a child, for example, will no longer have to keep their eyes glued on the CGM trending info because the computer is doing it for them. The computer, insists Brewer, does a better job of that anyway. "What we'll do is let them know if that number is trending in a way that is a problem, and then they can get involved."

Figure 1

Bigfoot's *smartloop* Automated Insulin Delivery System

Source: Bigfoot Biomedical

And, the same goes for physicians. "We're going to support a much more time-efficient and effective interaction with clinicians," says Brewer, "by doing a better job of providing more actionable recommendations." Doctors, he explains, don't have time to look at a lot of data. Instead, "they need to look at insights and get advice and recommendations. We're going to try and distill that data into actionable outcomes" so they can have meaningful conversations with their patients in the short amount of time allotted for patient visits.

Security is another important aspect of AP system development that Bigfoot is taking very seriously, and that is something that also differentiates the company from its competitors, says Brewer (**Johnson & Johnson**, for example, recently publicly acknowledged cybersecurity concerns around its *Animas OneTouch Ping* insulin pump). "You have to use state-of-the-art talent and technologies in order to make sure you have a secure connection. And you have to design that in from the ground up." Others may try to bolt-on security after the fact, but that type of solution ultimately won't be safe in a connected world, he says.

The end-result, says Brewer, is a system of components "smartly designed" to work together. "We're not an insulin pump business," he notes, "and we're not a sensor business. We're a systems business. And that means we're going to try and have the best-in-class. We're building a system that brings all these things together and makes them easy to use and upgradable." In fact, he continues, Bigfoot's system is designed to be over-the-air firmware upgradable, similar to smart phone operating systems today.

Finding a New Business Model

In addition to bringing together a range of sophisticated and user-friendly technology solutions, Bigfoot is also re-envisioning the AP business model. Much of that work is based on Brewer's early realization that moving this market forward would require a business model very different from what medical device companies had relied on in the past.

Bigfoot's model centers on bundling all of its components into a service: patients will get one prescription and make one co-pay, and all of the devices and supplies needed to manage the disease, in exactly the right quantities, will come to them automatically on a monthly basis. That's nothing short of revolutionary compared with the multiple prescriptions and multiple steps required to keep up with this disease today. It's as big a change as the AP itself, notes Brewer.

"There's tremendous waste in the system today," he points out, and device companies are going to have to make a lot changes to meet the demands of consumers and payors in the future. Today, doctors often overprescribe diabetes supplies so that patients never run out, but that leads to a stockpile of supplies that often expire before patients can use them all. What Bigfoot is doing, he explains, is absorbing that risk. "We're going to give the patient exactly what they need when they need it—because we will have perfect information about what they need [through our data collection]." And that's why, he adds, the connected system is so important. "We will know every time a patient pricks their finger; we'll know every time they change their infusion set; we'll know how much insulin they're using. So we're going to do it smarter, with less waste, and pass that savings on to the insurance company and the patient."

Moreover, the company will be providing its "smart" just-in-time inventory management solution without requiring a large up-front cost. That is vastly different from the current model. Today, insulin pumps typically sell for about $6,000 up-front, and the patient may have to shoulder 20% of that cost to satisfy their co-pay. Bigfoot intends to upend that model with a monthly service fee and no up-front cost. Moreover, the company plans to tie its monthly fee to outcomes measures that are of value to payors, including parameters such as HbA1c levels and time-in-range. "We built a modeling infrastructure such that we can model outcomes for different patients," says Brewer. With that information, the company can go to payors and tell them exactly how Bigfoot can improve their current patient outcomes. "We're

going to literally tie the price of this service to those outcomes and put money at risk." This type of shared risk and shared savings is new to the diabetes community, Brewer says, because never before has there been a system capable of sufficiently simplifying and automating the process.

Brewer believes this model could add up to significant cost savings, not only in terms of the devices themselves, but particularly with regard to adverse events—such as hospitalizations for hypoglycemia, for example—that he believes the Bigfoot system will help avert. "We're developing a system that, through this holistic design of troubleshooting software and Cloud-based monitoring, is going to dramatically remediate these events, which are very traumatic for the patient and very costly for the healthcare system."

Innovating from the Ground Up

Going up against much larger, well-entrenched competitors won't be easy, but Brewer believes Bigfoot will be able to offer a much more robust, user-friendly solution. And, one of the primary reasons it can do that, he says, is because Bigfoot, unlike the Medtronics of the world, is not constrained by the limits of traditional thinking and existing technology. "We're free to innovate from the ground up."

The company recently completed a Series A funding round for a total of $35.5 million, led by Quadrant Capital Advisors, and including Cormorant Asset Management, Senvest Capital, and Visionnaire Ventures. With its *smartloop* system already in clinical trials, the young firm clearly has come a long way over the course of only two years.

Notes Brewer, "We're tying together the best-in-class devices and we're making them smarter and secure, so that in a world where every aspect of our lives is connected, we can leverage that same kind of power for the treatment of this very burdensome disease. And that's a very different approach."

Medtronic and Abbott Score Important FDA Approvals in Diabetes Device Space

Late last month, FDA handed down two device approvals that have important implications for the US diabetes device market. First and foremost, the agency approved **Medtronic plc**'s PMA for its *MiniMed 670G* hybrid closed-loop insulin delivery system, the first such device to reach commercialization. The *670G* is a treat-to-range system that combines a *MiniMed* insulin pump with Medtronic's new *Guardian Sensor 3* (formerly called the *Enlite 3*) seven-day continuous glucose monitoring (CGM) technology and its *SmartGuard HCL* algorithm. Together, those components form what is commonly referred to as an artificial pancreas (AP)—a system that automatically adjusts insulin delivery from the pump based on the patient's individual CGM readings and glucose trending information. In the case of the *670G*, it is a hybrid, treat-to-range AP, which means that it adjusts insulin delivery to target a pre-set blood glucose level (120 mg/dL; can be adjusted up to 150 mg/dL during activity). It is not a completely automated, hands-off device—patients must still enter information on their carbohydrate consumption, make manual bolus insulin adjustments, and periodically calibrate the sensor with blood glucose measurements. However, it is the closest yet to that hands-off goal, and thus its commercial entry represents a milestone for the AP space.

The FDA approval came several months earlier than expected—and just three months after Medtronic's PMA submission. The company is currently gearing-up production and expects to begin shipping the *670G* in spring 2017. As part of the approval, FDA is requiring Medtronic to conduct a post-market study of the device under real-world conditions. It is currently FDA approved for use by people age 14 and older with type 1 diabetes, but Medtronic hopes to eventually expand that to younger children and is performing clinical studies of the system in children age 7-13.

According to Danielle Antalffy, an analyst with Leerink, the faster-than-expected FDA decision could bode well for other new products in the AP and CGM arenas and hasten further progress in the AP field. However, exactly how quickly the *670G* will gain traction in the US market, once it's launched, remains to be determined. Reportedly, Medtronic plans to price the device similar to its current pump/CGM combination systems, and patients who already have the company's new *630G* pump can upgrade to the *670G* at a reduced price. But even if current Medtronic pump users come on board at a good clip, there could be some hurdles convincing physician prescribers of the system's merits for new patients.

Some physicians have expressed skepticism about Medtronic's sensor accuracy, according to Antalffy, writing in a Sept. 28 research note, and sensor performance will be "key to adoption" of this technology. That negative perception, she noted, is based primarily on "historical Medtronic products," and doesn't reflect direct experience with the new *Guardian Sensor 3*, but "it does highlight the perception hurdle that Medtronic faces given its historically less accurate sensors vs. **DexCom**." (*See "DexCom Sets High Bar in Growing CGM Space," and "Taking Stock of CGM's Future: A Conversation with DexCom CEO Kevin Sayer,"* The MedTech Strategist, *August 24, 2016*.) Of note, in clinical testing, Medtronic's new *Guardian* sensor demonstrated an accuracy—expressed as MARD (Mean Average Relative Difference from a finger stick)—of 10.6% with

two finger stick calibrations per day and 9.6% with four finger stick calibrations per day. That compares to the DexCom *G5* CGM's still superior accuracy of about 9% with two calibrations per day (the *G5* is the current CGM market leader).

Antalffy expects strong growth going forward in the overall insulin pump and CGM markets, which she writes "are highly underpenetrated…leaving significant opportunity for broader adoption across many players." Larry Biegelsen, senior analyst for Well Fargo Securities, says the *670G* should help accelerate Medtronic's US diabetes business; he expects the company to post US diabetes growth of 10% in the second half of 2017, driven primarily by the *670G* launch.

Medtronic may gain a substantial first-mover advantage by being first-to-market with an AP system; however, there are several other companies nipping at its heels, including **Bigfoot Biomedical**, profiled in this issue (*see "Bigfoot Biomedical: Reimagining Diabetes Care with a Novel AP System"*), which hopes to file for FDA approval of its novel AP in late 2017 or early 2018. Like Bigfoot's *smartloop* AP system, Medtronic's *670G* has an algorithm that adapts over time, adjusting insulin dosing based on the individual patient's needs. However, unlike *smartloop*, the *670G* is not a connected device, thus the system doesn't provide remote monitoring or data sharing (Medtronic reportedly intends to build Bluetooth connectivity into future models). As a result, the *670G* does not currently integrate with a smart phone—all of the algorithms and functionality are fully integrated into the pump itself. That could be considered a plus or a minus, depending on the individual patient—it frees users from having to carry their phones with them, but those used to managing their lives with their smart phones may find the lack of integration an annoyance.

In addition to Medtronic's milestone *670G* FDA approval, **Abbott Laboratories'** Diabetes Care division appears to be closing in on its goal of obtaining US approval for the firm's long-awaited *Freestyle Libre* CGM. In September, the company received FDA approval for the *Freestyle Libre Pro Flash*, which is designed for professional/physician office use (the device is FDA approved only for use in people age 18 and older). At the same time, Abbott also announced that the consumer version of the device is now under FDA review, a process that could move along fairly quickly now that FDA has already approved the *Pro*. If that turns out to be the case, the consumer version, which is already on the European market, could reach the US sometime in 2017.

Abbott's *Freestyle Libre* technology strikes a middle ground between finger stick blood glucose testing and traditional CGM devices—it provides less functionality than existing CGMs, but it also costs substantially less and requires fewer components, and it offers more convenience than blood glucose testing (in fact, the device is designed to replace conventional blood glucose meters). The *Freestyle Libre* does not provide patients with real-time, continuous glucose trending information or the alerts and alarms they get with existing CGMs. However, the consumer version is likely to appeal to many patients. And, while it may be best suited to those with type 2 diabetes, some type 1s might find it appealing as well, which could put some competitive pressure on the traditional CGM space.

Like traditional CGMs, the *Freestyle Libre* measures glucose in the interstitial fluid (via a low-profile sensor system adhered to the patient's upper arm [Abbott is reportedly pursuing more discreet sensor insertion sites such as the stomach and thigh]). However, it uses a smaller sensor filament that some patients say is less painful to insert than existing CGMs. Although traditional CGMs continuously record glucose values, the *Freestyle Libre Pro* records glucose levels only once every 15 minutes, while the consumer version records glucose every minute. In the *Pro* version, the device is placed on the patient's arm in the clinician's office. Patients leave it on for 14 days, going about their normal daily routine (no finger stick calibrations are required), after which time, they return to the office and the physician removes the device and downloads the data for assessment.

In the consumer version, patients also wear the sensor for up to 14 days, but they can self-check their glucose levels on-demand by swiping a touchscreen reader over the sensor. The consumer version stores up to eight hours of data at a time, providing single glucose values as well as a trend arrow and an eight-hour glucose history. In Europe, the consumer system is approved for use without finger sticks, either for calibration or insulin dosing (with a few exceptions), which is a big plus for patients (the system is factory calibrated and has a MARD of about 11% with no finger sticks).

The consumer version of the *Freestyle Libre* has proven to be very popular in Europe. Once it reaches the US, the device is likely to find its greatest adoption among patients who are seeking a more convenient alternative to blood glucose testing but want something less costly than traditional CGMs. They are likely to be patients who want a system with enough functionality to reduce their disease burden, but one that doesn't overpower them with data and alarms. One caveat: the *Freestyle Libre* is not as accurate as existing CGM sensors when it comes to detecting hypoglycemia, and thus is not likely to be an ideal solution for patients with frequent hypoglycemic episodes or those with hypoglycemia unawareness. In clinical testing, according to Abbott, when the *Freestyle Libre Pro* gave a low glucose reading (at or below 60 mg/dL), 40% of the time the actual blood glucose value was in the 81-160 mg/dL range. US reimbursement for the consumer version could also prove challenging, notes Kyle Rose, an analyst with Canaccord Genuity, since the device is unlikely to fall under existing CGM benefits.

Data from the consumer version of the *Freestyle Libre* is expected to be downloadable to the patient's computer. And, importantly, Abbott recently introduced a new, Android-compatible mobile app in Europe called *LibreLink* that enables *Freestyle Libre* users to scan their device using their smart phone and share the data with clinicians and other caregivers.

—Mary Thompson