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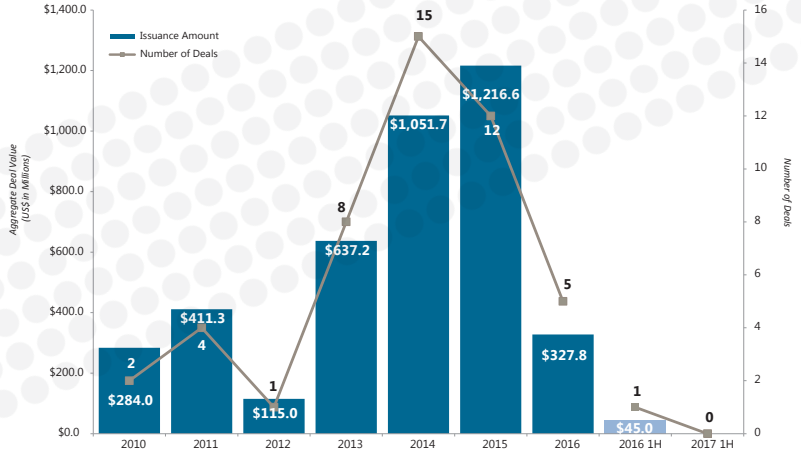

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Bigfoot and Abbott: A Match Made in Heaven?

An Interview with Bigfoot Biomedical CEO Jeffrey Brewer

Bigfoot Biomedical's recent deal to integrate Abbott's FreeStyle Libre glucose sensor technology into its automated insulin delivery system is a major step toward Bigfoot's goal of creating the most patient-friendly AP system possible, and it's a big vote of confidence in Abbott's Libre, which is designed to eliminate the need for fingerstick calibrations. In this Q&A, Bigfoot CEO Jeffrey Brewer lays out the rationale for the deal and discusses how this and other recent initiatives fit into the company's long-term, patient-centric vision.

by
MARY THOMPSON

Collaboration is the name of the game in the diabetes device field these days, and the past few months have certainly followed that trend, with a number of new deals announced recently (*see Figure 1*). Many are aimed at either offering patients more user-friendly data/disease management tools or establishing (or bolstering) a company's presence in the artificial pancreas (AP) arena, two huge areas of innovation that are already helping to shape the future of diabetes treatment.

For some small, innovative start-ups, collaboration/investment involving a large medtech player is the first step on the road to eventual acquisition. A recent deal of note in that regard is **Roche Diabetes Care**'s acquisition of Vienna, Austria-based start-up **mySugr GmbH**, announced in June. Founded in 2012, mySugr is a digital health company offering a popular, app-based data management platform for diabetes patients that automatically collects and manages data from a variety of devices (it is an open platform and will remain so, according to Roche)—including blood glucose meters and continuous glucose monitors (CGMs). Available in 52 countries with more than 1 million users worldwide, mySugr makes it easier for people to track their blood glucose readings and other information (such as carbs consumed, activity, insulin administered) in one location, see data trends/patterns, and share data with doctors and other caregivers. In 2016, mySugr launched a diabetes digital coaching service as well. Roche has partnered with mySugr since 2014 and was an investor in the company, so the acquisition was a natural next step. And, with the ongoing popularity of digital data management tools for diabetes, it is possible that a similar scenario could play out for **Glooko**, which offers another popular diabetes data management platform (**Medtronic plc** is a major investor in Glooko).

Deals in the AP space have also ratcheted up recently. For example, **Senseonics Inc.**, which has a 90-day implantable CGM that could be FDA approved before year's end (the company is working on a 180-day version), announced two collaborative deals over the past couple of months: one with Roche Diabetes Care and one with **TypeZero Technologies**—with the goal of integrating technologies from all three companies (Senseonics' *Eversense* implantable glucose sensor, TypeZero's *InControl* AP algorithms, and Roche's *Accu-Chek Insight* insulin pump) into an AP system. The integrated system will be tested in the NIH-funded, randomized IDCL (International Diabetes Closed Loop) trial, which is slated to complete enrollment in June 2018. The IDCL study will compare closed-loop vs. non-closed loop (with a separate pump and CGM) insulin administration, and will test both implantable and external CGMs in the AP arm. (*Editor's note: we'll have a more detailed update on Senseonics, along with several other diabetes device companies, in a future issue of* The MedTech Strategist.)

But perhaps the most interesting (and somewhat surprising) new deal in the AP space comes from **Bigfoot Biomedical**, which continues to demonstrate its willingness to break new ground in pursuit of the most patient-friendly solutions for people with diabetes. (*See "Bigfoot Biomedical: Reimagining Diabetes Care with a Novel AP System,"* The MedTech Strategist, *October 24, 2016*.)

In mid-July, Bigfoot announced a deal with **Abbott Laboratories** to integrate Abbott's *FreeStyle Libre* glucose sensor technology into Bigfoot's

automated insulin delivery platform. The agreement is a bit surprising because Bigfoot, up until now, has been working with **DexCom Inc.**, the market-leading player in CGM. (*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*.) A DexCom *G5* CGM was the sensor employed in Bigfoot's initial safety study, completed successfully last year, and most observers assumed it would be part of the final Bigfoot system, slated to enter pivotal trials in 2018. Analysts have described Bigfoot's move as a "missed opportunity" for DexCom, and rightly so, as Bigfoot is one of the most innovative companies in this space; however, DexCom still has plenty of other AP partnerships in place. In fact, DexCom supplies CGM sensors for the majority of AP systems currently under development (by companies other than Medtronic, which has its own CGM technology).

For Bigfoot, the deal offers an opportunity to further shake up the AP arena with the first integration of a sensor technology designed to eliminate the need for fingerstick calibrations. As such, it is one big step toward Bigfoot's goal of creating the most patient-friendly AP technology possible (to support those efforts, now that the CGM deal is in place, the company will conduct a Series B funding round, seeking $50-75 million). Bigfoot CEO Jeffrey Brewer also believes the two companies have a similar philosophical view of this market—like Bigfoot, Abbott really understands who the user of this tool will be—meaning the average person—he told the *MedTech Strategist* recently, and that user wants fewer burdens, not more.

For Abbott, the collaboration with Bigfoot is a major validation of its factory calibrated *FreeStyle Libre* system, which has proven hugely popular as a standalone sensor system outside the US—quarter/quarter growth for the consumer version in Europe has topped 20%, according to Matthew Taylor, an analyst with Barclays—due to its lower cost (compared with traditional CGMs), improved wearability (flatter sensor module), and elimination of fingerstick calibration, which is a huge plus for most patients. Bigfoot will be using a second-generation *Libre* sensor, and although Abbott has been mum on details, it presumably will allow the collection of continuous glucose data, which the current *Libre* system does not do. Along those lines, Brewer tells MTI that "Bigfoot will be taking advantage of the *Libr*e 2.0's ability to transmit real-time continuous glucose data to our system wirelessly."

One caveat: although FDA approved a professional version of the *FreeStyle Libre* last September (patients wear the device for 14 days and then return to their physician's office for analysis), the consumer version, which will enable patients to intermittently monitor their own blood glucose, has been under FDA review for nearly a year, which suggests FDA is taking a very close look at some of the data. Given the positive European experience with the system, a rejection from FDA seems highly unlikely; however, the agency does appear to have some safety concerns around sensor accuracy, particularly in the lower glucose ranges, and possibly as it relates to off-label use for dosing. And the device's MARD (Mean Average Relative Difference—a measure of accuracy compared to blood glucose readings) is substantially higher (in the 12% range) than DexCom's *G5* sensor (which has a sub-10% MARD). Despite FDA's cautious approach to the technology, Brewer says he is confident the *Libre* sensor will perform well, even in the hypoglycemic range, when integrated with his firm's algorithms and insulin delivery systems.

Meanwhile, Abbott continues to anticipate FDA approval and US launch of the stand-alone consumer *Libre* before year's end, although recent comments from company officials suggest that may get pushed out a bit. During Abbott's Q2 earnings call earlier this month, company CEO Miles White declined to forecast a launch date for the system. Given the fact that the *FreeStyle Libre* makes use of Abbott's proprietary process for factory calibration, which White said is "unique," he noted he wasn't surprised that discussions with FDA are taking longer than initially anticipated. Those talks are going well, he added, but "I never want to predict the FDA." That said, once the device does reach the US market, demand is likely to be very strong.

Of course, Bigfoot and others developing next-generation AP systems will eventually have to compete in this space with medtech giant Medtronic, the first company to reach the US market with a treat-to-range hybrid closed-loop insulin delivery system. However, the door appears to be open to companies that can deliver on the promise of a truly patient-friendly solution. Medtronic may be ahead in the AP game in terms of timing, but its first-generation offering, the *MiniMed 670G*, is, by most accounts, less than ideal from a patient's perspective. There's little doubt that the *670G* can help patients maintain better, more consistent blood glucose levels and help prevent hypoglycemic episodes (particularly during the overnight period)—there's now a wealth of data demonstrating that. However, as this first-generation AP device reaches more US physicians and patients (it was officially rolled out at this year's American Diabetes Association meeting in June and is in a controlled launch in the US), it has increasingly come under fire for being too burdensome and difficult to use.

Specific comments on the *670G* appear to focus on the CGM sensor technology as well as training and operational burdens. Medtronic says the system's new *Guardian Sensor 3* CGM is the company's most accurate CGM yet, but patients and physicians are reporting that the system produces a lot of false alerts around sensor calibration. Moreover, there have been reports that the system often

kicks patients off of automatic/closed-loop delivery mode if they administer an incorrect bolus dose. The *670G* requires intensive patient training to manage properly as well as prescribing physicians that are well versed in the technology (which rules out most GPs), and even some tech-savvy endocrinologists have bemoaned the additional time and effort required of them to make sure patients are using it properly. As a result, some clinicians appear to be taking a cautious approach by recommending the device only to their most capable, motivated patients, which suggests that adoption of the *670G* may fall short of initial expectations.

That adds up to a first-generation system that, while highly anticipated by many people with type 1 diabetes, leaves a lot of room for future competitors to make improvements (Medtronic also has future iterations in the pipeline). And that opens up unique opportunities for a company like Bigfoot, which is focused on patient-driven issues.

Bigfoot's collaboration with Abbott is actually the second deal the company has done in the past couple of months. In early June, Bigfoot announced that it had acquired Patients Pending Ltd., maker of the *Timesulin* smart insulin cap technology for insulin pens. The company's first *Timesulin* product, on the market for about six years, is an insulin pen cap that tells patients when they took their last insulin dose (the aim is to lower the incidence of missed doses, which Patients Pending CEO John Sjölund says is a common problem). But Bigfoot's primary interest is in the firm's next-generation *Timesulin* technology, a Bluetooth-enabled dose-capture system for insulin pens that is able to capture and transmit data on how much insulin is administered with each dose. Bigfoot intends to integrate that technology with its insulin dosing algorithms, CGM sensor, and iPhone app, so that patients using insulin pens, and their physicians, can get a better handle on exactly how much insulin they are taking and how that is impacting their blood glucose levels. The system will provide dosing calculations and guidance and will track all of the data on the user's smart phone. In essence, it will offer the same functionality as

Figure 1

Recent Deals in the Diabetes Device Space

Companies Involved	Date	Specifics
Bigfoot Biomedical & Abbott Laboratories	July 2017	The two have entered into an agreement to develop and commercialize an automated insulin delivery system (aka AP system) that utilizes Abbott's *FreeStyle Libre* glucose sensor technology, which does not require fingerstick calibration.
Bigfoot Biomedical & Patients Pending Ltd./Timesulin	June 2017	Bigfoot acquired the maker of *Timesulin*, a "smart" cap technology for insulin pens.
DexCom & Apple	June 2017	The two are collaborating to enable data from DexCom's CGMs to go directly into the Apple Watch without having to first pass through the iPhone.
DexCom & Ascensia Diabetes Care	July 2017	Ascensia's *CountourNext One* blood glucose meter will be bundled with DexCom's *G5* CGM for Medicare patients using CGMs.
Insulet, Medtronic & Glooko	June 2017	Insulet and Medtronic participated in Glooko's $35 million Series C funding round. Glooko has a popular diabetes data management platform that interfaces with a variety of devices. Medtronic, which also co-led Glooko's $16.5 million Series B round, may be positioning itself to acquire Glooko.
J&J/LifeScan* & Qualcomm	June 2017	LifeScan will use Qualcomm Life's *2net* connectivity solution to streamline wireless data capture from LifeScan's *OneTouch Verio Flex* blood glucose meter.
Roche Diabetes Care & mySugr GmbH	June 2017	Roche has acquired mySugr, a mobile diabetes platform that combines a popular app for automated data tracking with services such as diabetes coaching and unlimited test strips, and that integrates with a number of diabetes devices. Roche has partnered with mySugr since 2014.
Senseonics & Roche Diabetes Care and Senseonics & TypeZero Technologies	July 2017 May 2017	Senseonics inked deals with Roche and TypeZero aimed at collaborating on an artificial pancreas system. The system will integrate Senseonics' *Eversense* implantable glucose sensor, TypeZero's *InControl* AP algorithms, and Roche's *Accu-Chek Insight* insulin pump.
TypeZero Technologies & Cellnovo	April 2017	TypeZero's *inControl* AP software will be incorporated into Cellnovo's Bluetooth-enabled insulin micropump with the aim of constructing an AP system.

*J&J is currently evaluating strategic alternatives for its under-performing diabetes business units.

Source: *The MedTech Strategist*

Bigfoot's pump-based automated delivery system, except that instead of a pump that automatically adjusts and delivers the insulin dose, patients will administer their own insulin using the smart pen, with guidance from Bigfoot's dosing algorithms.

Bigfoot's ultimate aim with both of these deals is to give patients more choice and to make living with diabetes a lot easier than it is today. And with that in mind, the company also plans to up-end the existing diabetes device business model by offering patients and payors a one-stop shop of bundled components that will be provided as a service. Patients will receive one prescription and will make one co-pay (with no big up-front cost) and all of their chosen devices and supplies will be delivered automatically, as needed, on a monthly basis. That not only makes things easier for patients, notes Brewer, but it simplifies the process for physicians and payors too.

In the following Q&A, Bigfoot CEO Jeffrey Brewer discusses in detail the rationale behind the Abbott deal and the benefits he believes can be gained by offering an automated insulin delivery system that does not require fingerstick calibration. He also provides more insight into the *Timesulin* acquisition and how that fits into Bigfoot's longer-term vision for the business. According to Brewer, it's all about choice, patient empowerment, and ease of use, which explains much of the appeal of Abbott's *Libre* sensor. "When you take the usability into this," he notes, "not having to calibrate and not having to teach somebody to calibrate, not having to create mitigations for when they don't calibrate or they calibrate badly, makes for a simpler, easier-to-use system, and that's what we're all about."

The MedTech Strategist: ***Congratulations on your deal with Abbott—was this a long time in the making?***

Jeffrey Brewer: We've been working on this for a long time and now we finally got all the pieces to go and build something pretty disruptive, and so we're thrilled.

MTS: ***How did this all come about? You've had a longstanding agreement with DexCom for its CGM sensor technology, what drove you to look for a new sensor partner?***

Brewer: We had a development agreement with DexCom, which allowed us to trial a system using their sensor—that's the first step. Then once you figure out you've got something you want to take to market, you need to work out a commercial agreement that anticipates pricing, support, all sorts of collaboration on the regulatory process—just a more complicated relationship.

We were in a very advantageous position where competition had brought itself to bear. DexCom was one of the companies we talked to, but there were a number of parties at the table—some you may know, some you might not—and the commercial terms were relatively equal, so they weren't the deciding factor. We could have had a deal with a number of different parties that would have been conducive to building this business. This decision was made purely as an affirmative choice by Bigfoot for what we believe will be the safest, best [glucose sensor] system that's going to create the most disruptive business.

MTS: ***Abbott has had a lot of success with its*** *FreeStyle Libre* ***sensor system outside the US (the consumer version is awaiting US FDA approval and a professional version was FDA approved last year—****see "Medtronic and Abbott Score Important FDA Approvals in Diabetes Device Space,"* ***The MedTech Strategist,*** *October 24, 2016****). A good part of the appeal among patients centers on the fact that the*** *FreeStyle Libre* ***does not require fingerstick calibration. And, assuming FDA agrees with this labeling when it grants final approval to the consumer version, that's likely to be a big selling point in the US, since fingerstick calibration is required of every CGM sensor currently on the US market.***

However, the *Libre* ***sensor has a substantially higher MARD (Mean Average Relative Difference—a measure of accuracy compared to blood glucose readings) than CGMs that require fingersticks, particularly DexCom's current*** *G5* ***CGM, which is widely recognized as having the lowest MARD currently available. Are you concerned that*** *FreeStyle Libre****'s higher MARD might impact sensor accuracy in your closed-loop system?***

Brewer: We have come to understand over time that all MARDs aren't created equal. There is a theoretical MARD that some companies report based on clinical trials, but you have to understand how you can achieve that MARD, especially when it requires fingerstick calibration. Some companies will claim that they have 9% MARD, but let me tell you what you have to do to get to that. You have to calibrate with a fingerstick a couple of times a day at least, but when you're doing that you have to do the following procedure, which is reliably done in a clini-

cal trial or highly controlled environment but not at all in the real world. You have to wash your hands, that's the first step. Most people don't do that. After you live with the disease for some period of time, that's the first thing that goes out the window. Second, you're supposed to use an alcohol swab to prepare the site after you've washed your hands, and then let everything dry. Then you're supposed to prick your finger and use the second, not the first, drop of blood because the first drop might be contaminated by whatever's on the surface of the skin or what you just washed your hands with. And then, you never calibrate around the time you exercise or after you've eaten or if your glucose is rising or falling.

So if you do all of those things, which few people do reliably, then you can get a 9% MARD, and if not, you're talking 15-20% on a real-world average, if not worse. Because, in reality, people don't take the time to do all of this. In fact, a lot of people will just lick their fingers to prepare the site. Or they don't calibrate at all. Sometimes they will actually give the CGM a number that it just gave them—so they calibrate the CGM with the CGM just to silence the alarm, which as you can appreciate, would be very dangerous if it were off by some wide measure. And if that were tied into a closed-loop system, it might give them an insulin dose that might put them at risk.

This has been a learning process for us, but our analysis and data modeling shows us that mis-calibration is the biggest risk to a closed-loop system—it literally is the biggest safety concern. If you can do away with calibration, you can make systems much safer. So while the MARD of the Abbott *FreeStyle Libre* sensor is nominally 12%, it doesn't change based on mis-calibration. And I'll take 12% over everything else that exists today all day long, because in the real world, where people actually use these systems, that is the best you're ever going to do. And if you do better in the future, great, but that's good enough.

MTS: ***That seems to run contrary to what a lot of people believe about CGM accuracy, though. Is there data out there supporting this?***

Brewer: People like Bruce Buckingham, a well-known pediatric endocrinologist at Stanford, have presented data showing how problematic calibration is in the real world. And that's one theory for why we believe that first-generation closed loop systems will experience challenges in the marketplace: they will require too much interaction and engagement and it's mostly around calibration. I think any system that's built on a sensor that requires calibration is going to be equally problematic. That's the fundamental insight that we had that led us to go with Abbott because this is going to be a better closed-loop system.

You know, if you put people in a bubble and observe them washing their hands and using alcohol swabs and taking the second drop of blood, then you can get a certain result, but it's meaningless to the healthcare problem that we're trying to solve. This is the difference between medical device companies that are historically focused on doctors and trained, credentialed medical professionals and people who read manuals and listen to instructions, and the real-world experience of ordinary people who are busy and only semi-engaged in their own disease management. It's a very different kind of challenge from a design perspective.

MTS: ***As I understand it, you're going to be using a second-generation*** *FreeStyle Libre* ***sensor. What will be different about that sensor compared with the current*** *FreeStyle Libre****?***

Brewer: In order to be able to communicate as part of an insulin delivery system, the next generation of *FreeStyle Libre* will include a real-time communication technology. Outside of that, Abbott is not yet disclosing details of the next-generation product.

MTS: ***Getting back to this issue of sensor accuracy, it seems like you're saying MARD doesn't matter. But there are CGM sensors that require fewer calibrations than others to achieve a low MARD—aren't they inherently more accurate?***

Brewer: Well, I can only look at what is. So, if I put a calibration-requiring sensor next to one that doesn't require calibration and I give it to ordinary people and don't actually look at how they use it, the one that doesn't require calibration—the *FreeStyle Libre*—is going to be more accurate.

My contention is that the calibration and the concern about calibration is one of the drivers for why the existing AP products that are approved are so cumbersome and require such user engagement. And I don't think that's going to improve with another sensor.

But you have to also remember that what you're required to do for calibration with a stand-alone CGM system may be different, from the FDA's perspective, than what you do with a [closed-loop] system. If you only have a sensor, you have to have a way to measure accuracy. But if you have a system, then the measurements become more intuitive—like, is it keeping people in the safe glucose range more often and do they go into hypoglycemic range far less? And

if we use those measures, then MARD goes away. Because I'm talking about the stuff that really has a direct bearing on quality of life and healthcare costs.

MTS: ***How are you going to convince physicians of this? Will you need comparative studies? Because right now, it seems like endocrinologists (and some patients) value a low MARD.***

Brewer: We're going to test it in our pivotal trial. But, for me, comparing stand-alone sensors is beside the point. A sensor by itself is not very useful for the broad population, that's why we're doing what we're doing. We think when you have insulin data and glucose data and food data all together, you can be much smarter. So I have no interest in proving that one sensor is hypothetically better than another, because when you take the usability into this, not having to calibrate and not having to teach somebody to calibrate, not having to create mitigations for when they don't calibrate or they calibrate badly, makes for a simpler, easier-to-use system and that's what we're all about.

We intend for our system to be easier to use, require less training and less work, with the goal that patients are going to be safer. We need to lower the cognitive and emotional burden of this disease with fewer things to think about, to learn, to train, to do, and then you can reach more people. Of course, there is room for a number of solutions. What we're doing is very differentiated. I'll let everyone else fight for MARD supremacy, I just want something my son will use.

MTS: ***Abbott is breaking new regulatory ground with its factory-calibrated*** *FreeStyle Libre****, and FDA apparently has some concerns about the accuracy of the consumer version, which has been under FDA review for nearly a year now. Abbott is currently conducting studies to validate the system's accuracy, apparently to address those concerns, but there's no guarantee that FDA will approve the device with its current labeling. Might this add to Bigfoot's regulatory burden or risk down the road? Is there a chance that FDA will require patients using your AP to perform periodic fingersticks anyway?***

Brewer: Doing away with fingerstick calibration is truly paradigm changing. Big steps forward such as *FreeStyle Libre* will always generate more regulatory scrutiny. That is the cost of being first and driving the field forward. At the end of the day, given the FDA's demonstrated track record of support for innovation in diabetes, it is a question of when, not if, Abbott gets approval. So I have no concerns about *FreeStyle Libre* being approved. The data demonstrably supports that dosing insulin off of *FreeStyle Libre* is as safe, if not safer, than other sensors requiring calibration. In a closed-loop system, removing the need for calibration has an even more pronounced benefit in usability and safety.

> ***Our analysis and data modeling shows us that mis-calibration is the biggest risk to a closed-loop system—it literally is the biggest safety concern. If you can do away with calibration, you can make systems much safer.***

MTS: ***Will the new deal with Abbott impact your product development/regulatory timeline?***

Brewer: The deal does have one downside. It's going to take longer, which is hard because as you know this is personal as well as professional for us. My kid's going to be the first customer once our solution is approved. He's 22 and he won't actually use a product like those he could buy today because they require too much work and effort—if it's beeping at him all the time, he just won't do it. This is what he needs and now it's going to take us between six and twelve months longer to do it [to integrate and customize the algorithm and system with the new sensor—and get FDA's buy off on that]. That was not an easily arrived at decision, but it is the right decision for the long term.

MTS: ***When we spoke at ADA, you said you hoped to begin a pivotal trial of the AP system early enough in 2018 to file a PMA in Q1 2019, with possible market launch that year—so this pushes that all out by 6-12 months?***

Brewer: Yes, that's my best guess right now. [*Editor's note: the company still expects to begin its pivotal trial in 2018, but this new timeline pushes the PMA filing out to late 2019 or early 2020, with commercial launch in late 2020, at the earliest*.]

MTS: ***Let's talk a bit about your longer-term vision and how your recent acquisition of Patients Pending Ltd., and its*** *Timesulin* ***smart insulin pen cap technology, fits in with***

that vision. There is already a* Timesulin *insulin pen cap on the market that keeps track of when the last insulin dose was given, but as I understand it, the company also has a new cap product—a Bluetooth-enabled dose capture technology that can measure how much insulin was taken with each dose and then transmit that data to a smart phone or the Cloud.

Our vision is to offer choice to accommodate different people, different doctors and their preferences, and also different payors and what they're willing to pay.

Brewer: We're approaching this from a consumer perspective, so we believe there needs to be variety and choice in terms of insulin delivery systems. Some people will wear an insulin pump and a CGM and some people won't attach anything to their bodies—they prefer shots and are only going to prick their fingers. Some people prefer a tethered pump that has a tube, so you can infuse insulin on the stomach and store the pump somewhere else, out of sight. Other people like patch pumps that don't have a tube. Today, you either have to be a patch pump person or a tethered pump person or a shots person. Why can't you be different things across time? Why can't you have choice? For a disease that is so lived by the patient, in terms of the decisions and the self-care, it needs to be more consumer-friendly.

And the same type of choice should be available in sensor technology. Because a certain part of the population would like an implantable sensor and they're willing to have a surgical procedure. That will work better for them. And some other people might not want that, and the increasingly convenient minimally invasive options will be good enough. My vision is that we will have a minimally invasive sensor option and then we will have an implantable as an option as well.

Our acquisition of Patients Pending and its dose-capture technology will allow us to offer more choice. If you want to be on shots, we'll help you take the right amount of insulin with shots because the *Timesulin* smart cap technology will allow us to capture the information about how much short- or long-acting insulin people are injecting with insulin pens. Today, that data doesn't exist in a system such that you can actually help people titrate insulin appropriately—to tell them how much *Lantus* they should be taking, or how much at a meal they should be taking for a given number of carbs. The machine-learning technology that we've developed for our automated system, which enables it to automatically infuse insulin, is the exact technology that could help us tell you how much to take in that shot.

So our vision is to offer choice to accommodate different people, different doctors and their preferences, and also different payors and what they're willing to pay. This is the only thing we think really makes sense. There need to be different solutions for different people; different levels of disease engagement.

We want to support as much technology and as much of this ability to help as is digestible by all three of those constituencies—patients, physicians, and payors. And this is the thing that's hard about building these businesses. You can't just focus on one of those customers, you have to focus on all three of them at the same time. I don't think there's anybody else who actually started from this patient-focused standpoint before. And when you do, you start to think about how the consumers use the devices more than about how the doctors think they use the devices.

MTS: ***How do you view the smart pen opportunity and how do you plan to integrate your technology with the* Timesulin *smart cap?***

Brewer: You're going to hear a lot more about smart pens and connected insulin injection. The problem for people who are on injections is their doctors have no idea how much insulin they're taking. The only way they would is if the patient kept a log, which even if they did, is probably highly inaccurate if you look at people's ability to transcribe all this information. So this is a big problem, and the way you solve this would be for the big insulin suppliers [Sanofi, Eli Lilly, and Novo Nordisk] to add some connected capabilities to the insulin pens they make so that you can get that information to your smart phone and into the Cloud. The problem is, we don't see them doing that anytime soon. Because those insulin injectors that they sell that are disposable—they basically give those away with the insulin. They have hundreds of millions of dollars of tooling in place for manufacturing these and any additional cost, even in pennies, breaks the model. The insulin business, I believe, is going to be disrupted in the future—biosimilars are coming—but nobody has the incentive in the existing model to create that ability to capture insulin data. There are some people who've developed very siloed solutions where you're using insulin cartridges, but it only gives you a very small part of the market.

John [Sjölund, CEO of Patients Pending] solved the problem by creating a cap that has the very clever technology to sense the volume of insulin remaining in an insulin pen. So you basically take the cap off, give yourself an injection, and put the cap back on, and it's able to sense the difference in the insulin and send that information to the phone such that we know how much insulin was given. And you can do it for a bunch of different types of insulin—for the basal insulin you're taking, for the mealtime insulin. It's the only way to solve the problem on a broad basis, and if you pair that with a CGM you'll have complete glucose and insulin data for most people who are taking insulin. And then, if you add our machine-learning technology, it basically determines, based on glucose profiles, what your carb ratio should be, what your insulin sensitivity factors should be, what the amount of basal insulin should be that you're taking on a daily basis. The phone will be a key part of the system. The system for the dose capture will basically be two dose-capture devices (one for basal and one for bolus insulin), a CGM, a BGM, and a phone.

This will be a revolution. Getting people on the right amount of insulin is a huge challenge in our current healthcare system. It's really just a math problem if you have the data, but today the data doesn't exist. So this is essentially the same software we're using for our closed-loop, pump-based system, but with a new insulin delivery mechanism.

And this fits in well with our vision of choice. Our system will even allow a person to switch back and forth from shots to pump and vice versa. And that type of flexibility also provides a unique solution for payors. We can go to a payor and say 'We have the solution that you can offer to anybody who is taking insulin. We have different price points, different form factors—people who want to be on pumps, people who want to take shots, people who will use a CGM, people who won't—we have it all. And Bigfoot will be a provider who gives you all the pieces for one prescription.'

MTS: ***What's your development timeline for the smart pen system?***

Brewer: The pivotal trial anticipated to begin in 2018 will be for our automated insulin delivery system. We will be doing separate trials for MDI [multiple daily injection] auto-titration, also utilizing Abbott's *FreeStyle Libre*. The timing for the MDI auto-titration trial is still under discussion, subject to feedback from the FDA, and we will be evaluating our commercial timeline based on this feedback. But as a company comprised of so many people directly affected by diabetes, we are impatient to deliver our solutions to market as quickly as possible.