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Advent Of Artificial Pancreas Tech To Galvanize Fast-Growing Diabetes Market

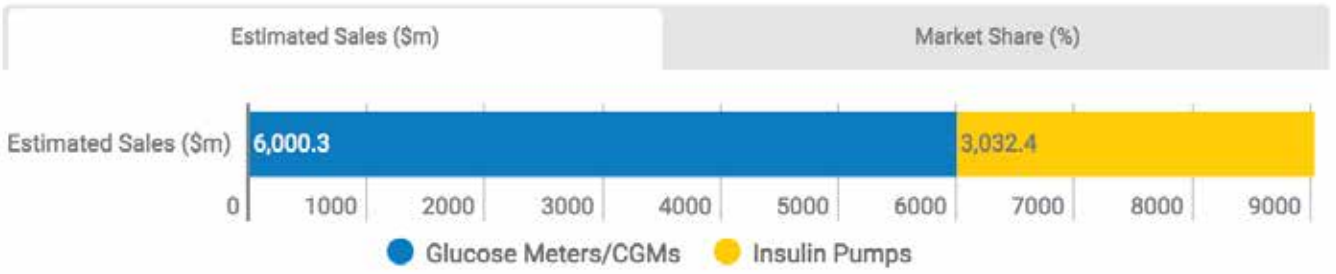
Executive Summary

The global diabetes management devices market is expected to exceed $11.2bn by 2020, driven largely by the rising diabetes epidemic. This, in turn, is fueling significant innovation such as next-generation, automated artificial pancreas systems and miniaturized, less-invasive wireless technologies that can continuously track and analyze glucose levels in real-time. This feature looks more closely at these and other potentially groundbreaking new technologies, as well as the competitive landscape of the two major product segments – insulin pumps and blood glucose monitors.

The global diabetes management devices market is expected to grow from $9bn in 2015 to $11.2bn by 2020, a CAGR of 4.5%. While blood glucose monitors – continuous or otherwise –account for the largest product segment of the total diabetes market with about 66% 0of total sales, the smaller, yet highly innovative insulin pump segment is expected to see the biggest growth.

According to a new report by Meddevicetracker, "Global Diabetes Management Devices Market," global sales of glucose meters and CGMs are expected to rise from roughly $6bn in 2015 to $7bn in 2020, a CAGR of 3.2%. This is driven partly by the vast majority of both Type 1 and Type 2 diabetics using these devices as an integral part of their daily glucose monitoring routine, compared to a smaller number of severe Type 1 diabetics having to rely on insulin pumps. However, continued pricing pressures have put a damper on the glucose meter segment and there has been a greater adoption of next-generation insulin pumps, which are expected to drive growth of this segment. Total insulin pump sales are expected to jump from $3bn in 2015 to nearly $4.2bn by 2020, representing a higher CAGR of 7%, compared to glucose meters. (See Figures 1 and 2.)

Figure 1. Global Diabetes Management Devices Market, estimated share by device segment, 2015



"Global Diabetes Management Devices Market," Meddevicetracker

Medtronic To Hold On To Pump Lead

Analysts predict that one of the key growth catalysts in the insulin pump segment will be Medtronic PLC's first artificial pancreas, the MiniMed 670G, which is expected to hit the US market this spring, as well as continued sales of previous-generation systems by Medtronic and other insulin pump makers in the US.

Medtronic has long dominated the global insulin pump market with its long-established MiniMed brand. According to Meddevicetracker estimates, in 2015, Medtronic held a 61.5% market share in the global insulin pump market segment with about $1.8bn in sales, and has been working to continuously improve upon existing products.

Last September, Medtronic won US FDA approval

for the newest member of the MiniMed family, the 670G insulin pump, which is described as the world's first artificial pancreas device-based system. The integration of SmartGuard technology, which automatically and continuously delivers the body's required insulin level, and "Suspend Before Low" technology, which allows for the pump to automatically suspend the release of insulin prior to reaching preset lows, is claimed to be the only system available in the US that safeguards against low blood sugar events.

First FDA Approved Insulin Pancreas

While the 630G and 530G are best-selling insulin pumps, Medtronic's MiniMed 670G is expected to revolutionize insulin delivery therapy for millions of Type 1 or insulin-dependent diabetics who are 14 years of age and older (Also see "US FDA Approves First 'Artificial Pancreas' In Medtronic's MiniMed 670G" - Medtech Insight, 28 Sep, 2016.).

Set to hit the US market this spring, the 670G is unique in that it is a fully integrated pump and CGM sensor with no need for a separate smartphone or CGM device. The device features Medtronic's SmartGuard HCL algorithm and the new Guardian glucose sensor, which allows up to 7 days of wear and offers the highest mean absolute relative difference (MARD) rating of 9.64% based on 3-4 calibrations per day, using the Ascensia Contour Next Link 2.4 meter, used for calibrating the CGM, and for remote bolus/insulin dosing.

In a pivotal trial, published in October in the Journal of the American Medical Association,124 patients with Type 1 diabetes (aged 14 years and older) used the device for 12 weeks. Study results showed that glycated hemoglobin levels fell from 7.4% at baseline to 6.9% at the end of the trial while their daily dose of insulin rose from 47.5 U/d to 50.9 U/d. The percentage of sensor glucose values within the target range changed from 66.7% at baseline to 72.2% at the end of the study, which is fairly significant. No episodes of severe hypoglycemia or ketoacidosis occurred.

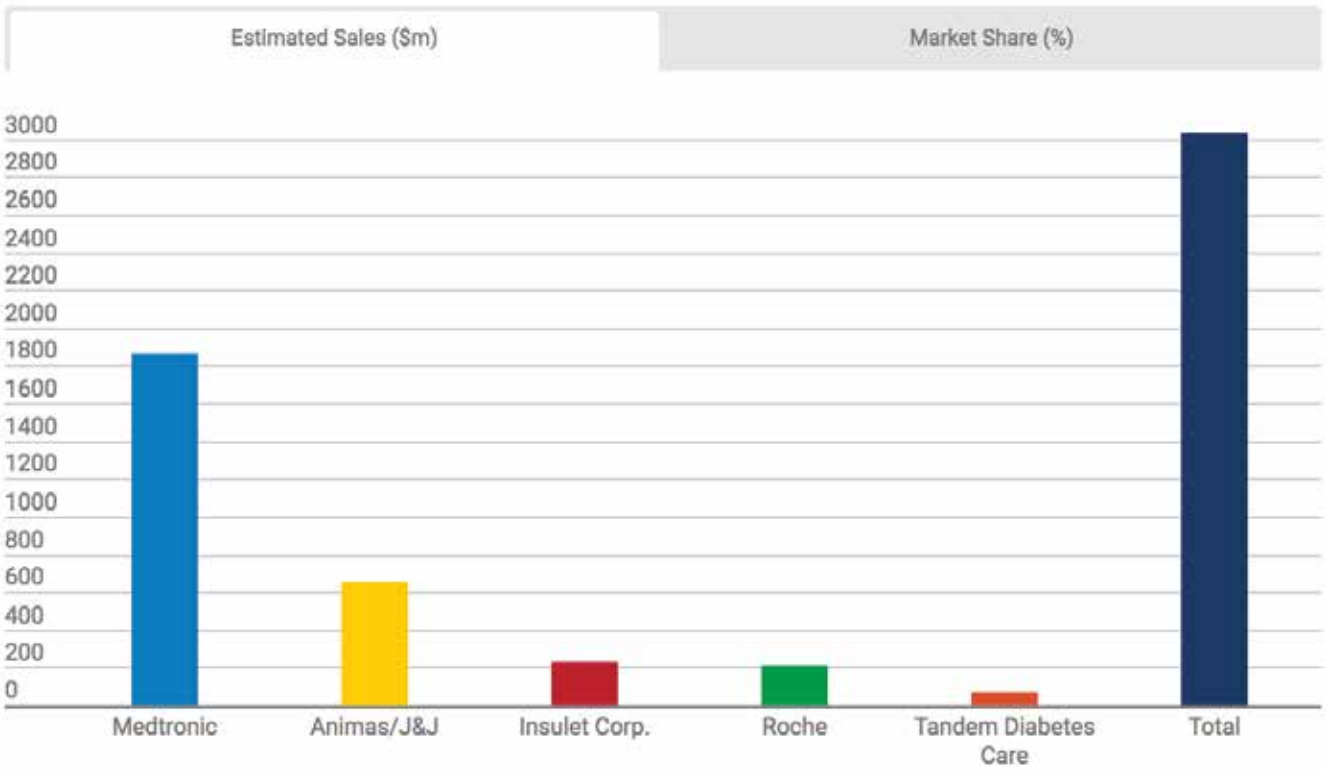
Meddevicetracker expects that the MiniMed 670G will drive Medtronic's diabetes devices sales over the next five years, barring any adverse events. The company said that after a limited initial commercial launch in spring 2017, it plans to gradually increase sales as insurers provide coverage, and expand its manufacturing, training and marketing efforts. Those efforts will likely also be bolstered by the device's expected marketing approval outside of the US in the summer of 2017, which Medtronic estimates will translate into a 10% sales growth in the second half of this fiscal year.

To entice customers to make the switch to the new device, following marketing introduction this spring, Medtronic said it would offer existing customers the opportunity to exchange their previous generation MiniMed 630G insulin pump system for the MiniMed 670G system (retail price is $799) for a $500 exchange credit, leaving an out-of-pocket cost of $299, according to Meddevicetracker. The company is also offering a six-week free trial for purchases of either the MiniMed 530G or 630G.

Meanwhile, sales of previous-generation MiniMed pumps, such as the MiniMed 530G/630G in the US and international models that are showing good growth in markets outside of the US, contributed to better-than-average Diabetes Group sales growth of 6% in the fiscal year 2016.

Medtronic, however, is expected to lose some market share in the coming years to some smaller, though aggressive competitors offering distinct features and improved or less invasive designs.

Figure 2. Insulin Pumps Global Market, share by supplier 2015



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Competitive Pump/AP Market

Ranking a distant second on the global insulin market is another giant in the diabetes market, Johnson & Johnson Animas Corp., which offers a portfolio of insulin pumps, including the OneTouch Ping and Animas Vibe System. In 2015, J&J's Animas Corp. had an estimated $655.6m in sales, accounting for a 21.6% share of the global insulin pump market.

The company's OneTouch Ping is a two-part glucose management system that includes the OneTouch Ping Insulin Pump and a meter remote. The pump and remote communicate wirelessly to automatically and continuously administer pre-set basal insulin and to check blood sugar. The system is designed to calculate how much bolus insulin is required to deliver insulin from the pump without the user needing to touch the pump, from up to 10 feet away. What makes the OneTouch Ping system also stand apart from other pump systems is its ability to count carbs and store nutritional value of 500 foods in a CalorieKing database. Besides OneTouch, the company also markets the Animas Vibe System, which won FDA approval in 2014, and is the only system available in the US for children as young as 2 years of age.

More recently, Johnson & Johnson has also joined the trend to miniaturize and offer patients less-invasive technologies. In 2012, the company acquired the OneTouch Via patch through its buyout of Calibra Medical Inc. The disposable waterproof patch, which is slated to hit the US market this year, is designed as an alternative to standard insulin pens and syringes to deliver rapid-acting, or bolus, insulin at mealtimes. Users simply press two buttons to deliver the insulin bolus, even through clothing, which makes insulin delivery convenient and discrete; and studies have shown that it increases patient compliance, particularly in social mealtime situations. According to results from a Market Acceptance Evaluation (MAE) study, the OneTouch

Via improved dose compliance in more than 50% of patients.

However, one major drawback of the Via is that it doesn't administer a basal rate of insulin, meaning those on multiple daily insulin injections must still administer their basal injection using standard pens and syringes, according to Meddevicetracker.

Although originally approved by the FDA in 2012, the OneTouch Via is the next-generation system of the Calibra Finesse. In 2015, Johnson & Johnson initiated a new trial enrolling 280 patients to assess the change in A1C, glycemic control and quality of life compared to using insulin pens over 24 and 44 weeks. Results of the trial are expected to be published this October.

Meanwhile, another giant, Roche, which ranks fourth in the insulin pump global market with $212.8m in sales, accounting for a 7% market share, is known in Europe for its Accu-ChekInsight Insulin Pump Therapy System; it's the first insulin pump that gives users the option to use a prefilled cartridge, which lessens the steps of having to fill or insert a new cartridge. The all-in-one system includes a handheld remote control and blood glucose meter that uses Accu-Chek Aviva test strips and Accu-Chek Bolus Advisor. In fiscal year 2015, Roche reported strong revenues, an increase of 8%, derived from insulin delivery devices in Europe of the relatively new Accu-Chek Insight, which was launched in the UK in 2014. The device is not yet available in the US.

While Medtronic remains king in the global insulin pump market for now, Meddevicetracker expects that the introduction of competitive innovative AP systems by 2018 is likely to disrupt Medtronic's monopoly in this segment.

AP Systems In The Pipeline

About a half dozen companies are collaborating with major diabetes medical device companies such as Dexcom Inc., a major player in the CGM field, to co-develop proprietary next-generation AP systems that will directly compete with Medtronic in the next few years (see Table 1).

Table 1. Selected emerging AP systems and expected launch 2018/2019

Company	Device	Expected Approval/Feature
Beta Bionics	iLet and Dexcom CGM	Phase II study in progress; expected approval 2018/2019
Bigfoot Biomedical	Smartloop Diabetes Management System	Phase I trial results pending; expected approval late 2018/early 2019.
Cellnovo/TypeZero	Artificial pancreas	Claimed to be the first patch pump and mobile connected system; combining mobile connected insulin patch pump with TypeZero's inControl AP software and Dexcom's CGM.
Cellnovo/Diabeloop	Artificial pancreas	Phase II study complete by end of 2017; expected CE Mark 2018. Three-component system including a patch pump, CGM and handset integrated with Diabeloop software; features capability to adapt to everyday variables, such as diet, exercise and stress.
Insulet Corp.	Omniopod Horizon	Feasibility study in progress; expected completion April 2017; approval expected 2018/2019. Hybrid closed-loop artificial pancreas system.
Tandem Diabetes Care/Dexcom/TypeZero Technologies	Smartphone-driven artifical pancreas	International Diabetes Closed Loop Trial complete by early/mid 2018; expected approval 2018

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Among them are Insulet Corp., which ranks third in the insulin pump global market with an estimated $277.1m in sales in 2015, accounting for a 7.5% market share and Tandem Diabetes Care Inc., which had $72.9m in sales in 2015, accounting for a 2% market share in the total insulin market, ranking it in fifth place.

Among the other notable players currently working on AP systems are Cellnovo Group, TypeZero Technologies, Beta Bionics and Bigfoot Biomedical Inc.

All of the companies mentioned above are working with Dexcom, which developed the G5 Continuous Glucose Monitoring System, the first FDA-approved mobile CGM for patients 2 and older, to integrate the technology into their pumps.

Medtronic is the only company so far that has commercialized a proprietary hybrid closed-loop pump and CGM system, automating two key components of an AP with unique safeguards that prevent glycemic events, which allowed it to bring the first AP system to market, Medtech Insight reported earlier (Also see "Dexcom Glucose Test System Approved For 2-Year-Olds" - Medtech Insight, 20 Dec, 2016.).

According to Meddevicetracker, two companies, Cellnovo and Tandem Diabetes Care expect to be on the marketplace with their systems by 2018, with Insulet Corp. expecting possible approval in 2018 as well.

It's too early to say who will win the race to the artificial pancreas market, but medical technology company Cellnovo and digital health company TypeZero Technologies announced on April 18 they completed a worldwide commercial license agreement to integrate and commercialize TypeZero's AP technology into Cellnovo's mobile diabetes management systems. No financial terms were disclosed, but the companies said that integration efforts are underway with an expected CE Mark and product launch in 2018. In a company statement, Sophie Baratte, CEO of Cellnovo, said, that "Our partnership with TypeZero brings us another step closer to delivering one of the first end-to-end diabetes management systems."

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TypeZero's AP software inControl AP was developed based on initial research by the Center for Diabetes Technology at the University of Virginia School of Medicine and will be incorporated directly into Cellnovo's Bluetooth-enabled micropump; the product, which is in early development, is claimed to be the first patch pump and mobile connected system. The artificial pancreas will be studied at the International Diabetes Loop Trial (IDCL), funded by the Institutes of Health.

Cellnovo is also partnering with French organization Diabeloop, which has developed an AP algorithm combined with the Cellnovo system for Type 1 patients over the age of 18. The three-component system, which includes a patch pump, CGM, and handset integrated with Diabeloop software, has the capability to adapt to everyday variables such as diet, exercise and stress. An initial trial of 36 patients showed positive results; a second clinical study of 60 patients at 12 centers in France is expected to be completed by November.

Another collaboration between three companies – Tandem Diabetes Care, Dexcom and TypeZero Technologies – for a "smart" AP system, also holds promise for a market introduction in 2018.

San Diego, California-based Tandem Diabetes Care entered into a license agreement with TypeZero Technologies to incorporate its technology into Tandem's next-generation t:slim Insulin Pump. The "smart" AP system alerts patients with recommendations including real-time advice regarding insulin basal rates, insulin bolus calculations and meals, and helps patients make better decisions regarding exercise. It also automatically controls insulin delivery and virtually eliminates hypoglycemia, allowing patients to gain tighter control over glucose levels. Another key component is the inControl Cloud system, which tracks patient data and offers real-time analytics, monitoring and notifications via telemedicine to caregivers, allowing for real-time intervention to prevent complications.

The system is currently being tested in a 120-patient NIH-funded clinical trial at the University of Virginia

Centers for Diabetes Technology and other sites, where the inControl AP will be compared to using a sensor-augmented insulin pump in Type 1 diabetics and evaluate how well glucose levels are controlled to the extent in which hypoglycemia is being reduced over a six-month period. The trial was slated to start in March and produce primary outcome results by January 2018.

Meanwhile, Insulet Corp., which stands apart with its tubeless pump technology, has developed a hybrid closed-loop AP system, OmniPod Horizon, which is currently being evaluated in a feasibility study in about 60 adults with type 1 diabetes. The study is expected to be completed this month. Earlier this year, Insulet announced positive results, reporting that the OmniPod performed well with no safety issues during day and night and was very effective, resulting in minimal hypoglycemia and excellent fasting glucose. Specifically, key findings showed that patients remained in the target blood glucose range 69% of the time over the 36-hour study, and maintained target blood glucose control 90% of the time during the overnight period. The company claims its competitive edge lies in the specialized algorithm, which originally came from a UC Santa Barbara Artificial Pancreas algorithm, and aims to anticipate the future rise or fall of blood glucose levels, reacting quickly to adjust insulin delivery to optimize outcomes in each patient.

Two smaller firms, Bigfoot Biomedical and Beta Bionics, are also hoping to win FDA approval next year or in 2019, for their respective AP technologies.

Last October, Milpitas, California-based startup Bigfoot Biomedical raised $35.5m in a Series A investment to support the final development of its smartloop automated insulin delivery system for Type 1 diabetics, which is uniquely delivered as a monthly medical device-based service. The company's integrated cloud-connected diabetes management system interfaces with wearable glucose monitoring and insulin delivery tools accessible via a secure mobile app on a smartphone.

Beta Bionics, a Massachusetts-based public benefit corporation, in partnership with Zealand Pharma, is developing a unique dual-hormone (insulin/glucagon) AP or "bionic pancreas" system, integrated into a pocket-sized wearable medical device called iLet. The dual-chamber system, originally developed by Beta Bionics at Boston University, combines automated insulin and glucagon with the Dexcom CGM and uses mathematical dosing algorithms. The company is seeking to recruit patients (expected enrollment is 20 patients) for a Phase II feasibility study at Massachusetts General Hospital to assess the safety and efficacy of the iPhone-based bionic pancreas in improving glycemic control in Type 1 diabetics. This February, Beta Bionics also received a $5m investment from Novo Nordisk to advance its fully integrated iLet device and make it compatible with the firm's NovoLog insulins, adding to an earlier $5m investment from another major insulin drug maker, Eli Lilly, Medtech Insight reported. (Also see "Number To Know...5,000,000" - Medtech Insight, 6 Feb, 2017.)

Blood Glucose Monitoring Devices

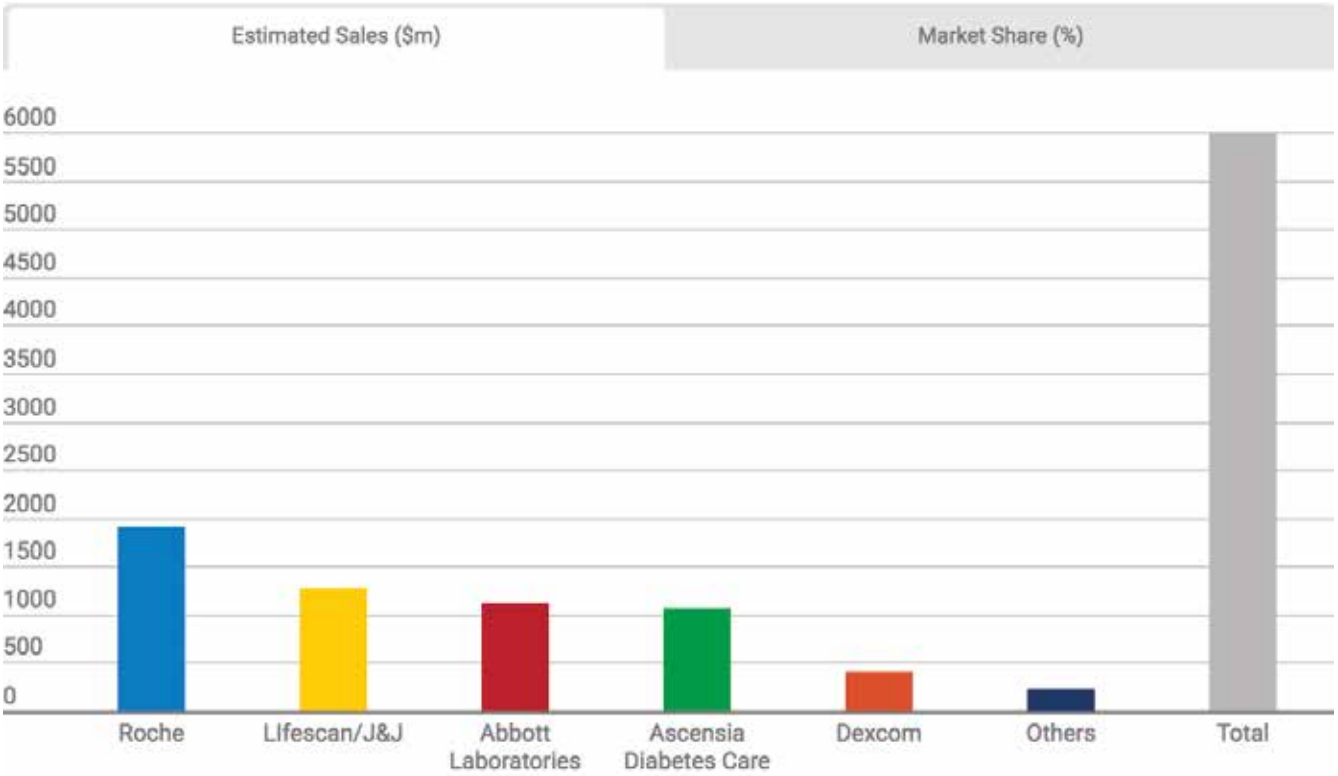
Blood glucose monitoring devices are essential for diabetes management to frequently monitor blood glucose levels, especially in Type 1 diabetics, but also in people with Type 2 diabetes, to better control the condition and improve outcomes.

The Big Four Leaders

The $6bn global blood glucose monitor devices market continues to be dominated by Roche and its Accu-Chek brand, which in 2015 had estimated sales of $1.9bn, accounting for a 31.9% total market share. LifeScan Inc.a Johnson & Johnson company, which also includes Animas Corp., a producer of insulin delivery systems, and Calibra Medical, which developed the OneTouch insulin patch pump (described earlier), ranked second in the global glucose monitor devices market with $1.2bn in sales in 2015, accounting for a 21.2% market share. Abbott Laboratories Inc., which offers a broad blood glucose monitoring system portfolio under the FreeStyle brand, ranked third in the same segment with $1.1bn in sales in 2015, which gave it a 18.6% total market share. Ascensia Diabetes Care, formed in January 2016 via the sale of Bayer Diabetes Care to Japanese Panasonic Healthcare Holdings Co. Ltd., which markets the Contour brand, ranked fourth with estimated sales of $1.1bn in 2015 and a 17.9% market share of the total glucose meter market. Dexcom, a smaller, but growing CGM competitor, ranked fifth with $400.7m in sales in 2015 in the global glucose meter devices market

in 2015, accounting for a 6.7% total market share. Other companies had sales of $220m in 2015 and a 3.7% market share in this particular segment. (See Figure 3.)

Figure 3. Blood glucose monitoring devices global market, share by supplier, 2015



"Global Diabetes Management Devices Market," Meddevicetracker

As mentioned earlier, while the global blood glucose devices market has been significantly larger than the insulin pump segment, Meddevicetracker expects it to grow at only about 3% over the forecast period – primarily due to recent revenue declines by Roche and other major competitors in 2015 and 2016. The declines resulted from severe price erosion amid a 2013 ruling by the Centers for Medicaid and Medicare Services to cut reimbursement rates for test strips, which has been a lucrative business.

Reimbursement Cuts for Test Strips

In an effort to significantly cut waste, fraudulent claims and to cut reimbursement rates, CMS enacted several cost-cutting initiates over the 2008-2013 timeframe. In particular, in July 2013, CMS cut reimbursement for test strips by 72% in July, which impacted Roche's diabetes care sales as well as rival companies. Roche's diabetes care sales reportedly declined 3% by $2.19 in 2015 from $2.39bn in 2014. While several diabetes device makers in this segment were hit hard by the ruling, the falling reimbursement rates have also led to a greater influx of lower-price competitors, which has put more pressure on companies to divest their business interest. One of these companies was Bayer, which in 2015 sold its Diabetes Care business to Panasonic Healthcare Holdings. In January, Johnson & Johnson announced it was also exploring the sale of its diabetes care business, citing declining sales.

Despite pricing pressures and price erosion, Meddevicetracker expects that the glucose meter segment will see a slight rebound over the forecast period. The main drivers will be the ever-increasing diabetes population, which fuels the demand for

glucose monitoring systems, as well as advances and increased usage of next-generation, stand-alone CGM technologies.

Continuous Glucose Monitoring Systems

CGMs started appearing on the marketplace less than 10 years ago, but have seen continued popularity, because they allowed people living with diabetes, primarily those with Type 1 diabetes, to gain a better understanding of glucose levels and trends. That is in addition to improving potentially dangerous night-time hypoglycemia and overall glucose control vs. traditional home-use glucose meters that provide a "snapshot" of glucose levels.

Typically prescribed by a physician, CGM systems measure interstitial glucose levels in real-time, 24 hours a day and require significant fewer finger sticks. However, most CGMs – with the exception of Abbott's new FreeStyle Libre Pro/Flash device – still require some finger stick calibration, and therefore don't replace self-monitoring glucose meters.

CGMs typically comprise four components: a CGM monitor or insulin pump with built-in capability, a transmitter that attaches to the sensor and wirelessly sends glucose data to the monitor or pump, a sensor inserted under the skin, and a push-button insertion device.

While the rising incidence and prevalence of diabetes is expected to boost demand for CGMs globally, technological advancements and integration with smart devices by tech companies like Apple, Inc. and others are driving this market segment forward.

The key players in the CGM segment are Abbott Laboratories, Dexcom, with its G5 Mobile, and Medtronic with its iPro/Enlite sensor used with the MiniMed insulin pump and Guardian Connect mobile CGM. However, these giants are facing increased competition from innovative companies including Nemaura Medical'ssugarBEAT and Senseonics Holdings Inc.'sEversense system.

Competitive Landscape

Considered a potentially disruptive technology due to its ability to totally eliminate finger sticks, Abbott's FreeStyle Libre Pro CGM, which gained FDA approval last September, uses a wearable sensor that measures glucose levels through the interstitial fluid for up to 14 days, but also has a companion reader device that scans over the sensor and reads current glucose levels in real-time.

Because the device is factory-calibrated, finger sticks are not required, which also makes it more cost-efficient. Patients still need to visit their doctor's office to get the sensor inserted into the back of the upper arm. The system allows doctors to follow hypoglycemic and hyperglycemic trends via the Ambulatory Glucose Profile (AGP), part of the FreeStyle Libre Pro Reader. The company recently announced that it has submitted a consumer version of the FreeStyle Libre CGM system to the FDA for review. This version includes a consumer glucose reader that allows the patient to conduct self-monitoring at home, and would further expand Abbott's market size.

Meanwhile, Dexcom, now a $570m-plus company (as of fiscal 2016) with high double-digit sales growth, is steadily advancing market share in the glucose monitoring segment, and has the only CGM on the market classified as "therapeutic" by CMS.

The company has been highly successful in aggressively leveraging its proprietary G5 technology via integration with diabetes device companies, including in the development of next-generation AP systems, as mentioned in the previous section.

Most recently, Dexcom has made some notable achievements, including:

- gained an indication for children as young as 2 years of age;
- gained coverage under Medicare Part B under durable medical equipment, making it the only CGM device that qualifies for this classification;
- received ground-breaking approval for "non-adjunctive" use (no longer requires supplemental use of home blood glucose meters to verify measurements, except for calibration).

Like other CGMs, Dexcom's G5, which gained FDA approval in August 2015, requires the insertion of a small sensor just below the skin's surface to continuously monitor glucose levels. It uses a transmitter to relay data to the Dexcom G5 Mobile app every 5 minutes via Bluetooth. The Share technology allows up to five care recipients to

constantly monitor glucose information, receive immediate alerts, and share glucose data and trends. The system is available on iOS devices, including the Apple Watch, and this year, is also expected to be available on Android devices. The company's next-generation G6 sensor is expected to be significantly smaller than the G5 and allows for one-handed insertion. It also includes a touch screen receiver interface and an improved app. While Dexcom has made significant inroads with expanded insurance coverage, established key partnerships and leveraged its proprietary technology, it too will be facing stiff competition from emerging technologies.

Germantown, Maryland-based Senseonics Holdings Inc. also developed innovative technology. The Eversense sensor is the first and only fluorescence-based implantable CGM sensor system that continuously measures glucose levels for up to 90 days, eliminating the need for weekly sensor insertions and daily finger sticks. The sensor is inserted subcutaneously in the upper arm and wirelessly communicates with a smart transmitter, which is worn on the arm, to relay data to a mobile device with a diabetes app. Unlike most competitive sensors – including those made by Abbott, Dexcom and Medtronic that need to be removed every seven days or slightly longer – the Eversense sensor can remain in place for up to 90 days.

According to Senseonics, the Eversense is accurate over the 90-day period at a MARD of 11.4% (over 4.2mmol/L or 75mg/dL). The other unique feature of the Eversense system is that the transmitter delivers a vibration at low or high glucose readings.

Last December, Roche expanded upon an earlier distribution agreement with Senseonics for the rights to market the Eversense product line to diabetes clinics and patients in most of Europe, the Middle East and Africa. The Eversense CGM system is approved in selected European countries and currently up for FDA approval.

Last November, Senseonics presented results of the PRECISE II US 90-day pivotal trial enrolling 90 patients at the 16th Annual Diabetes Technology meeting. The results demonstrated strong accuracy for the 90-day continuous wear period with a MARD of 8.8% across the 40-400 mg/dL range when compared to YSI blood reference values.

Meanwhile, UK-based Nemaura Medical sets itself apart from competitors with a needle-free system called sugarBEAT,which it hopes to debut in Europe this year. The company announced on April 24 it successfully completed the development and testing of its second-generation sugarBEAT wireless skin patch and plans to start clinical trials to submit CE approval mid-year, with a planned European launch later this year.

The sugarBEAT system relies on a disposable patch to draw interstitial fluid to the surface of the skin with electric currents. The sugarBEAT sensor connects wirelessly to a Bluetooth-enabled watch-like device and measures and displays glucose levels several times an hour – day and night. This information can then be easily transmitted to the doctor's office. Because the system requires only one daily finger stick test for calibration and offers audible alerts, the company touts its system as more cost-effective and convenient compared to available CGMs.

Interim clinical trial results presented in October 2015 from an ongoing 540-patient day clinical program of Type 1 and Type 2 diabetes patients showed a reduction in MARD from 18% to 11.8%. So far, the sugarBEAT system has gained the CE mark in March 2016 as an adjunct device. In the US, the company expects to finish clinical studies, then submit a PMA application mid-year.

One partnership that relies on the power of data, is also expected to make news mid-year. IBM Watson, which provides computerized health care solutions, and Medtronic joined forces to develop the Sugar. IQ app, which uses real-time continuous glucose and insulin information from Medtronic pumps and glucose sensors to provide real-time insights on hidden patterns.

In particular, the app is designed to uncover behaviors associated with glucose patterns and send alerts to patients. The app's Glycemic Assist feature also allows users to ask about specific foods or therapy-related actions and events to see how it may impact glucose levels, and has software to track food in a diary to provide meal-related insights and how they impact glucose levels.

A pilot study of 600 anonymous patients, using data from Medtronic insulin pumps and glucose

meters, showed that the Sugar.IQ was able to predict hypoglycemia up to three hours in advance – a potentially life-saving capability. The next phase calls for "real-world testing" of the final release, which is being conducted in up to 100 MiniMed Connect mobile accessory users to explore the design and usability of the Sugar.IQ app. The companies said they'll use the feedback from these users to plan for more extensive product roll-out mid-year.

Other Emerging Diabetes Care Techs

A slew of other tech companies, including technology giants Apple and Google Verily, have also established partnerships with leading diabetes device makers to try to create truly innovative technologies.

According to recent news reports, Apple has assembled a team of engineers dedicated to developing optical sensors to measure blood glucose without the need of finger sticks or piercing the skin. Apple is reportedly investing millions to develop these new technologies and is believed to have already run feasibility trials. The company has also formed several partnerships with leading diabetes device companies to try to integrate noninvasive glucose monitoring into wearable devices. Among them is Roche, which announced in March 2016, that it integrated the Accu-Chek Diabetes Management app with Apple's HealthKit app, available for iPhone users. The collaboration unites the two technologies, allowing the app to share glucose data with HealthKit, which also tracks carbs and other health and activity data.

Verily, Google's life sciences division, meanwhile, joined forces with Alcon Inc. /Novartis AG to develop a smart contact lens to measure blood sugar via the eye. The intent is for the minimally invasive smart glucose-sensing contact lens to continuously monitor glucose levels via tear fluid in the eye and connect wirelessly with a mobile device.

According to Verily, the smart lens contains miniature integrated circuits, sensors, and wireless communication capabilities for self-contained wireless sensing on the surface of the eye. Thus far, the work is still in its earliest stages. Verily also teamed up with Dexcom in 2015 to develop a miniaturized glucose-sensing device. (Also see "New GSK-Verily JV Aims For Smart, 'Grain Of Rice' Neuromod Tech" - Medtech Insight, 2 Aug, 2016.)

US FDA Approves First 'Artificial Pancreas' In Medtronic's MiniMed 670G

Executive Summary

The hybrid closed-loop automated insulin delivery system, the first closed-loop system approved anywhere in the world, automatically monitors glucose and provides appropriate basal insulin doses in people with type 1 diabetes.

A major milestone has been met in diabetes. US FDA announced Sept. 28 the approval of Medtronic PLC's MiniMed 670G hybrid closed-looped automated insulin delivery system.

It's the first hybrid closed-loop insulin delivery system approved anywhere in the world, according to the company, making it the first so-called "artificial pancreas," says FDA. (Also see "From Pipe Dream To Reality: Artificial Pancreas Set To Debut" - Medtech Insight, 16 Aug, 2016.)

Medtronic, however, says it will not begin commercializing MiniMed 670G until the spring of 2017 to provide time to ensure payer coverage, market and manufacturing readiness, and the training of employees, clinicians, educators and patients.

MiniMed 670G features Medtronic's SmartGuard HCL algorithm and the Guardian glucose sensor. It continuously delivers insulin at a variable rate in response to the patient's blood-glucose levels to maximize the time the glucose levels are within the target range. It requires minimal input from the patient. The user only has to enter information on their mealtime carbohydrates, accept bolus-correction recommendations, and periodically calibrate the sensor, Medtronic explains.

The FDA approval labels MiniMed 670G for patients with type 1 diabetes who are 14 years of age or over. The company is sponsoring a trial of the system in younger patients.

Medtronic believes it is at least three years ahead of any competitor in the development of an artificial pancreas. Wells Fargo analyst Larry Biegelsen says the approval is a big win for the company. "We expect the 670G system to help drive acceleration in Medtronic's US diabetes growth from the low-single-digits seen in the fiscal first quarter [reported Aug. 25]," the analyst writes in a Sept. 28 research note. "We currently model US diabetes growth of 10% for the second half of fiscal 2017, driven primarily by the 670G launch."

Keeps Patients In Target Glucose Range

At the American Diabetes Association conference in New Orleans in June, Richard Bergenstal of the Park Nicollet International Diabetes Center near Minneapolis presented data from a 123-patient pivotal trial that supported the FDA approval of MiniMed 670G.

Following a two-week control period during which the system's hybrid closed-loop functions was turned off, the patients used the MiniMed 670G for three months with the hybrid closed-loop functions operating as frequently as possible (a median of 87.2% of the time). No serious adverse events, diabetic ketoacidosis or severe hypoglycemia (low glucose levels) were reported during the study.

A comparison of the patients' sensor glucose levels at baseline and during the study phase of the trial showed that patients using the hybrid closed-loop system spent more time with sensor glucose between 71 and 180 mg/dL, less time with sensor glucose at 70 mg/dL or lower, and less time with sensor glucose at 50 mg/dL compared to baseline. Sensor glucose variability measured by coefficient of variation decreased from 0.38 to 0.35, a statistically significant improvement. Also, the patients' average glycacted hemoglobin decreased from 7.4 to 6.9, a significant improvement.

As a condition of approval, FDA is requiring Medtronic to sponsor a post-market study to better understand how the device performs in real-world settings. Once the device is launched in 2017, patients using Medtronic's earlier-generation MiniMed 630G system will be eligible to get a MiniMed 670G through a Priority Access Program.

Medtronic says it expects regulatory approval of the MiniMed 670G in territories outside the US in the summer of 2017.

FDA Speeded Process Along

Medtronic gained approval for a closed-loop system quicker than many would have expected several years ago. According to both FDA and the company, the US agency has devoted outsized time and resources to working with Medtronic on planning trial designs and other matters for this and precursor systems. (Also see "Medtronic Gets Extra FDA Attention To Hasten Approval Of Next-Gen Insulin Pump" - Medtech Insight, 24 Apr, 2014.)

In conjunction with this approval, FDA touted its role in working with a range of stakeholders, including multiple companies, to speed development of artificial pancreas device systems.

"The FDA has been working together with diabetes patient groups, diabetes-care providers, medical device manufactures, and researchers to advance the development of an artificial pancreas," the agency explains. "FDA's efforts include prioritizing the review of research protocol studies, providing clear guidelines to industry, setting performance and safety standards, fostering discussions between government and private researchers, sponsoring public forums, and finding ways to shorten study and review time."

On the same day as approval of the 670G, FDA also approvedAbbott Laboratories Inc.'s FreeStyle Libre Pro continuous glucose monitoring system for health-care professionals. (Also see "Abbott Gains US Approval For Pro Version Of Flash Glucose System" - Medtech Insight, 28 Sep, 2016.)

‘Selective’ JDRF Backs Israeli Injectable Blood Glucose Monitor

Executive Summary

An Israeli start-up developing an injectable, miniature continuous blood glucose monitoring implant has secured funding from the Juvenile Diabetes Research Foundation (JDRF) to speed up product development. The investment will be used to bring GluSense closer to its first in-human clinical trial.

An Israeli start-up developing a long term injectable blood glucose sensor for diabetics has scored $1.9m from the Juvenile Diabetes Research Foundation (JDRF) to bring the product closer to in-human clinical trials.

GluSense’s GlydeCGM, a miniature implant injected under the skin, is expected to last for one year, taking blood glucose measurements continuously and transmitting the data wirelessly to an external wearable device. Calibrated glucose measurements are then displayed on the wearable device and transmitted to a smartphone application.

The technology is still at an early stage but the firm – which emerged from the Israeli incubator Rainbow Medical – has already attracted several investors. To date, it has raised around $15m including financing from four Chinese investors - Ping An Ventures, ZTE, Keytone Ventures and Rongan.

“This [latest JDRF] investment is a huge recognition for us and our technology,” GluSense CEO, Boaz Brill told Medtech Insight. “The JDRF are very selective and it took time for us to convince them that this technology would really work. There was almost 10 months of due diligence until we got the green light so this is a huge win. Our main focus now is getting the product ready for clinical studies and this investment will help push the product out to humans.”

The JDRF T1D fund is a new venture philanthropy fund dedicated to supporting early-stage Type 1 diabetes treatments. Early animal tests of the device showed that the technology was able to provide high-accuracy measurements and long-term viability. The firm is now aiming to begin further pre-clinical studies in late 2017, then move to human studies in 2018. “The end goal is to have at least a one-year implantation, but we will start smaller with three months and six month studies,” said Brill.

“Hundreds of startup companies have tried to develop noninvasive glucose sensors and have all failed. The reason is because all of them had a very small, unspecific signal and were not able to deal with the noise of real life measurements. On the other hand, currently marketed Continuous Glucose Monitors (CGMs) are also inherently limited - they use an enzyme that takes up the glucose and creates electric charge based on interaction between glucose and oxides,” Brill explained. “But after some time you have issues when the glucose oxidase runs out or the tissue gets blocked or the oxide diffuses too slowly, which all affect the measurement.”

“The model GluSense is developing is completely different, it’s not based on an electrical measurement. Instead, we are setting out to provide a long term glucose sensor using an optical measurement, based on a fluorescent molecule.”

Glyde’s glucose detection uses a fluorescent protein that is sensitive to glucose and consists of three parts - two fluorophore groups and a glucose binding domain. As the glucose binds to the glucose domain of the fluorescent protein, the optical properties of the biosensor changes using the Fluorescent Resonant Energy Transfer (FRET) effect.

To overcome the challenge of maintaining long term sensor functionality, the device has been designed to include engineered live human cells that continuously replenish the fluorescent protein, ensuring fresh biosensor is always available. “We’re designing this product without any expiry date so we’re trying to make everything work if possible without any limitation,” said Brill.

The stable biosensor aims to free diabetics from the multiple calibration finger pricks currently needed for glucose measurement in CGM’s. “There are many products on the market right now for diabetes but they must be replaced frequently and require having

to prick your finger repeatedly. This is a very limited way to manage diabetes long-term for patients and our technology would minimize this need for frequent calibrations."

A physicist by education, GluSense CEO Boaz Brill, completed a PhD in Physics from the Weizmann Institute of Science in Israel and spent several years in the semi-conductor industry before heading into medical devices. "I was looking for a new adventure and medical technology seemed to me like the most interesting and fulfilling thing and the best way to apply my skills and experience in developing high accuracy measurement tools," he said.

"We believe that we have a really groundbreaking technology that could be viable for very long-term use and now with the help of the JDRF we can finalize development to help improve the life of people living with diabetes."

Dexcom First To CGM Reimbursement Finish Line

Executive Summary

Following a recent approval for their G5 continuous glucose monitor for use in children and adults without a finger stick, Dexcom has scored big with a new US Centers for Medicaid and Medicare Services policy that would make their CGM the first of its kind eligible for reimbursement from the agency.

Dexcom Inc. will benefit from a new ahead-of-schedule ruling from the US Centers for Medicaid and Medicare Services providing coverage for continuous glucose monitors (CGM) defined as therapeutic by the agency. The firm says its G5 CGM is currently the only CGM on the market that meets CMS' requirement that the device can be used to make treatment decisions.

"This landmark CMS ruling will make available the most important technology in diabetes management to the Medicare population," Dexcom President Kevin Sayer said. He says over the next few months the firm will work with CMS to implement the rule.

Immediately after an FDA advisory committee in July overwhelmingly recommended approving the test as a replacement for finger-stick glucose meters for patients aged 2 and older, Dexcom VP Steven Pacelli told Medtech Insight that the firm was working aggressively to gain reimbursement. But the first step to getting coverage was getting US FDA approval. (Also see "FDA Panel Overwhelmingly Votes For Dexcom CGM to Replace Finger Sticks" - Medtech Insight, 21 Jul, 2016.)

"It's somewhat up to CMS," he said at the time. "We'll work with CMS to decide whether they want us to go immediately to a national coverage decision ... or in some instances CMS will advise you to go on more regional basis first, and then come back for a national decision. My hope is we have reimbursement sometime in 2018."

Last month, FDA approved the Dexcom's test, stating it could reduce the burden of disease management. (Also see "Dexcom Glucose Test System Approved For 2-Year-Olds" - Medtech Insight, 20 Dec, 2016.)

"FDA recently approved expanding the indications of one CGM product to include replacement of blood glucose monitors for diabetes treatment decisions," states CMS in its ruling. "This ruling addresses whether 'therapeutic' CGMs, which provide information that can be used to make diabetes treatment decisions, meet the definition of DME. For the purpose of this ruling, all CGMs that are approved by the FDA for use as adjunctive devices to complement, not replace, information obtained from blood glucose monitors in making diabetes treatment decisions are referred to as 'non-therapeutic' CGMs."

CMS says the fee schedule for CGMSs such as the G5 will range from $236 to $277 per device.

"This coverage decision is well ahead of expectations ... and we believe it positions the company for potential upside to just-issued 2017 sales guidance of $710M to $740M," said Leerink analysts Danielle Antalffy and Rebecca Wang in a Jan. 13 research note.

Analysts caution it will take time to negotiate with regional Medicare Administrative Contractors. The reimbursement scheme isn't expected to be implemented until the middle of this year.

Nonetheless, the ruling gives Dexcom a leg up over competitors Medtronic PLC and Abbott Laboratories Inc.

"[Abbott] is pursuing a dosing claim for its already-filed Libre, but we believe sensor accuracy will have to improve ... before one is granted," the Leerink analysts state. "And as far as we know, [Medtronic] is not pursuing a dosing claim as of yet for any of their sensors or integrated pump systems."

Roche Exits Insulin Pumps Segment In India

Executive Summary

Roche Diagnostics has exited the insulin pumps segment in India, but the Swiss multinational says it stays focused on the self-monitoring solutions segment for diabetics in a country that has more than 69 million people living with the chronic disease.

Roche Diagnostics, the market leader in India's IVD industry, has confirmed it has moved out of the insulin pumps segment in the country. According to the company, the insulin pump is not extensively used in India as a solution for people with insulin-dependency.

The Swiss multinational said it would like to "focus" on providing people with diabetes self-monitoring solutions that will help them have a "good quality of life."

"We firmly believe that with regular self-monitoring, the vast population of people with diabetes in India can keep their blood glucose levels in check and lead normal lives without becoming insulin-dependent. Our exiting the insulin pumps segment in India is to fully concentrate on the SMBG (self-monitoring of blood glucose) segment," Sidhartha Roy, business unit head (diabetes care), Roche Diagnostics India, told Medtech Insight.

Roche's Accu-Chek Spirit Insulin Pump has not been available in India since 2011, but the company has been servicing insulin-dependent diabetics in India with the Accu-Chek Combo system right up "until a few months ago."

Roche confirmed that the Accu-Chek Combo system will not be available in India hereon. The Accu-Chek Combo system combines a blood glucose meter with an insulin pump that can exchange data in both directions via Bluetooth wireless technology; it supports a more targeted therapy management and also permits discrete insulin administration without the need to touch the pump, a 2012 Roche statement notes.

The company's latest generation insulin pump, Accu-Chek Insight, has not been launched in India, it said.

Asked whether Roche would continue to assist/service patients who have been using its insulin pumps in India or whether they had been transitioned to other products, Roy said: "Simultaneous to the decision of exiting the insulin pumps business in India, we initiated the process of transitioning our pump users to another similar product available in the country. The transition process has been completed with utmost care."

Cost, Service Support

Some experts say that while insulin pumps offer significant convenience and can deliver more accurate amounts of insulin compared with the syringe, the cost factor has been a significant deterrent especially in emerging markets like India.

While the exact prices of insulin pumps in India could not immediately be ascertained, industry experts say they are in the region of INR200,000 ($2,999), excluding the associated recurring costs for insulin supplies and accessories. That is within the same price range as a Nano, the small car from the Tata group's stable in India.

Roche acknowledged that the factors attributing to the low use of pumps by insulin-dependent diabetics include the "relatively high cost" of an insulin pump and the "service support" required to maintain it.

"For India especially, service support has been a major factor, considering the vast geographical spread of the country," Roy said.

An expert with a frontline multinational devices firm told Medtech Insight that insulin pumps per se have not been a very viable business in India because of the "huge connect" required between patients and the company.

"The patient has to be 'owned' by the company; there is a huge service component and margins are

not attractive," the expert said, adding that only few markets in the Asia Pacific are really feasible for such products in general.

Of the total population of people with diabetes in India, only 5% have type 1 diabetes, and of this, less than 1% are reported to use insulin pumps. These pumps typically deliver insulin from a reservoir inside the pump to a patient's body using an infusion set and a tiny cannula.

Building Awareness

While Roche's diabetes care business has seen lower worldwide sales in the first half of 2016, the Asia-Pacific and specific countries like Brazil, China and India have reported significant growth in the overall diagnostics business, an investor presentation in August indicated. (Also see "Roche Ends 2015 On Brighter Emerging Markets Note" - Scrip, 1 Feb, 2016.)

On whether the exit from insulin pumps in India is perhaps part of an effort to weed out the less sustainable businesses in the region, the company said Roche Diabetes Care in India "strategically focuses" on offering self-monitoring solutions to people with diabetes, to enable them to lead normal lives.

"Our efforts are concentrated on building awareness amongst the young population of people with diabetes in India so that their quality of life can be maintained with regular self-monitoring and specialist advice. This is the need of the hour for people in India, given the alarming levels of diabetes prevalence in the country," Roy added. Roche believes such awareness initiatives will also enable the healthy and young people of India to focus on healthy eating, fitness and regular checks of their blood glucose levels, to avoid diabetes due to lifestyle reasons.

There has been some past speculation that Roche may put its diabetes testing business on the block globally, though a news agency report in May this year quoted the top brass of Roche Diagnostics Corp. as underlining the group's commitment to the business and its growth potential.

Roche's awareness efforts in India are also in sync with the overall thrust of the Indian government in the area in view of the mounting burden of non-communicable diseases (NCD) in the country. India has initiated an integrated National Program for Prevention and Control of Cancers, Diabetes, Cardiovascular Diseases and Stroke focused on health promotion and prevention; strengthening of infrastructure including human resources; early diagnosis and management; and integration with the primary health-care system through NCD cells at different levels for optimal operational synergies. More recently, India's Ministry of Health and Family Welfare, in collaboration with the WHO Country Office for India and other partners, rolled out a mobile health initiative for the prevention and care of diabetes.

Sanofi Joins Google's Verily In Diabetes Venture

Executive Summary

Sanofi's diabetes head says French drug maker's joint-venture pact with Google's Verily will combine novel therapies for the condition with cutting edge technologies to produce better focused, outcome-based combinations.

A joint venture established by Sanofi and Google parent Alphabet will combine medicines, devices and software into an extensive diabetes care product line, according to the head of the French drug maker's global diabetes franchise.

The US-based JV, named Onduo, was announced Sept 12 as an alliance focus on helping type 2 diabetes patients better plan their day-to-day medication management and habits. Based in Cambridge, Mass, Onduo plans to eventually focus on type 1 diabetes, as well as to people at risk of developing diabetes, helping them to better prevent the onset of the disease.

Aim Is Joined-up Health

"Healthcare hasn't been very good at advancing connectivity so far. Diabetes is an excellent area to pursue and promote this, given the extent to which diabetics use the combination of drug and device, but for the most part there's very little connectivity there," Stefan Oelrich, who heads Sanofi's diabetes franchise, told Scrip.

He said Google parent Alphabet and Sanofi plan to invest about $500m in a joint venture. The joint venture will be independent but can draw on its parents' resources. Sanofi hopes the partnership with Alphabet's Verily Life Sciences will also promote novel ways that diabetes can be monitored and treated, and in the process help the French drug maker better adapt to a changing and increasingly competitive market. (Also see "'Challenging Quarter' For Sanofi As Questions Hang Over Diabetes Franchise" - Scrip, 29 Jul, 2016.)

But Onduo will also have the freedom to work with other diabetes product makers.

"Onduo has the right to do work with other pharma companies, and when seen in the solutions perspective we – Sanofi – don't have all the drugs that a physician needs for any given solution, so it is perfectly legitimate that the joint venture as it seeks outcomes solutions will also turn to medicines other than Sanofi medicines. That also reflects the different emphasis of this approach. When focusing on a certain desired outcome, then that may require other drug classes that we do not offer," Oelrich said.

Oelrich, 48, told Scrip that the JV will bring technology and targeted diabetes therapies together with the focus on outcomes. In essence the aim is for innovative medicines to be "joined-up" with delivery and monitoring technologies.

"What we have today are the medicines in their various formats – orals or injectables or self-administered pens along with glucose measuring systems and digital platforms that let someone for example count your carbs at certain times of the days that let you titrate better, and so on and so forth; but all of these are pretty much used in isolation and one is separate from the other and so what Sanofi and Verily thought was that together we could start introducing a much higher level of connectivity between existing solutions and upgrade those in terms of technology – which can mean miniaturization as well as connectivity," Oelrich said. "So you can, conceivably, connect an insulin pen to a CGM or a pump to a CGM that's connected to the correct insulin, as well as other solutions. You can think of integration with numerous apps that will coordinate all of them. That's where this may be going."

The end result could eventually be moving from product-centric to outcomes-based offerings.

"It's turning the current model or approach upside down. That frees us up from thinking just in terms of product portfolio and rather to desired outcomes," he said. Sanofi is investing $248m in cash in Onduo while Verily is committing an "equivalent" amount, he added.

Asked when Onduo might have its first product ready, Oelrich replied "We're aiming for a product within the next two to three years. That's in sharp contrast to our pharmaceutical research and development timelines of between five to ten years so this promises to be faster."

Regulatory approval time frames should not be too much of a problem either, he said.

"If you really link a medicine to a technology then there is a strong chance that you'll get a needed drug-type approval by the FDA. There is the chance they may want clinical studies before approval, but there are also digital solutions that don't require approvals what so ever."

The first proto-type product from Onduo "might involve integrating a pump, a constant glucose measuring system and a drug in a near autonomous system that optimizes insulin delivery. But that's up to Onduo," he said.

Other Therapy Areas?

The joined-up approach could eventually be applied to other therapy areas.

"You could think of all kinds of therapy areas where this could also apply. The interesting part of diabetes is we have 400 million people out there that live day after day with the condition. But I can well imagine this thinking for other therapeutic areas as well," Oelrich said.

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In August, Google life sciences spinout Verily announced it was partnering up with GlaxoSmithKline PLC for a spinout venture focused on bioelectronic devices called Galvani Bioelectronics. Bioelectronic medicine is a new scientific discipline that seeks to treat a number of chronic diseases including diabetes, asthma, arthritis, and inflammatory bowel disease by using miniature devices implanted in the body that are able to modify the electrical signals of nerves in the body. (Also see "GSK And Google To Invest £540m In UK-Headquartered Bioelectronics JV" - Scrip, 1 Aug, 2016.)