CLOSER LOOK

MEMORANDUM

WaveForm (AgaMatrix) shares CGM details: 14-day wear, no receiver, ~1 cal/day, 11.1%-13.9% MARD in 4 trials; CE Mark in 2018; Touts "vertically integrated" AID system - January 17, 2018

Executive Highlights

- **AgaMatrix Holdings' WaveForm Technologies recently announced its in-development CGM's ambitious feature-set (acquired from Bayer/iSense):** 14-day-plus wear-time, average one calibration per day (it will launch with one per day in Europe), no receiver (BLE smartphone communication), limited interferences (e.g., acetaminophen), one-hour warmup time or less, and "painless" insertion. The company believes it has a "competitive manufacturing cost profile," in line with its update in October. See a picture of the system below from the DTM poster. Execution and manufacturing scale will be crucial, as other players move ahead quickly on form factor, minimal/no calibration, accuracy, longer wear, reimbursement, and published outcomes.
- **WaveForm's CGM underwent four clinical trials in 2017, tested in a total of 57 patients, performing with a MARD of 11.1%-13.9%.** None of the studies tested 14-day wear, however: one was seven-day wear, one was 10-day wear, and one was a seven-day head-to-head trial against Dexcom's G5 (n=10). A trial in the second half of February will investigate 14-day wear. The data seem promising; while it's too early to know if this is what could be expected from the commercial product, we'll be eager to watch the progress.
- **Development of a "vertically integrated" automated insulin delivery system is ambitiously expected to begin this year.** The company tells us that it intends to ultimately own or have a pump built, and is in the process of finalizing a license of a basic algorithm, which will be modified in the coming months in advance of initial studies.
- **A CE mark for the CGM is still expected in 2018, in line with the October update - in new news, the company appears confident it can also launch the product in Europe in 2018.** Clinical trials to support a PMA submission to FDA could begin as soon as 2019 so this is yet another product that will be much further ahead in Europe than the US.

WaveForm Technologies - the company owned by AgaMatrix Holdings, LLC -just shared via press release the ambitious feature set of its in-development CGM system, targeting CE mark in 2018. The update included topline accuracy results from three 2017 trials (MARD 11.1%-13.9%), and plans to begin developing a "vertically-integrated" closed loop system in 2018.

The announcement characterizes the sensor, based on technology acquired from Bayer/iSense, as having a wear time of "14 days and longer"; "average" of one calibration per day (the EU launch will be one per day, though the WaveForm team tells us it envisions one/two on day one, followed by one per day or potentially one every other day); Bluetooth smartphone communication (no receiver); one glucose measurement per minute; one-hour warm-up time or less; "limited interferences" (e.g., acetaminophen); and "painless" insertion. Management believes factory calibration may be feasible - perhaps in a second-gen product or potentially by the time US approval and launch comes around - and, notably, emphasizes the importance of not rushing simply to satisfy a marketing hope or a claim. We got our last look at the sensor, transmitter, and computer mouse-esque applicator in a poster at DTM (below). The company believes it has a "competitive manufacturing cost profile." Of course, the bar is enormously high and only rising in CGM - execution will be crucial over the next couple of years. If WaveForm can deliver on this feature set - along with a very small on-

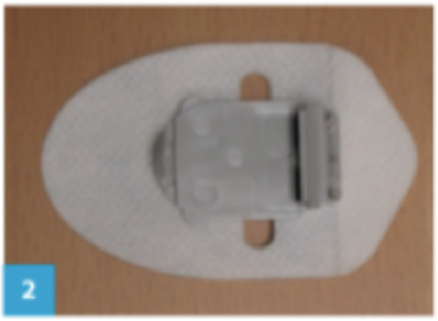
body footprint, a great app experience, and ideally a disposable transmitter - it could be competitive in a growing market.

In addition to eight trials in 292 patients conducted by Bayer prior to AgaMatrix's acquisition, the CGM was tested in four trials in 2017, three of which enrolled a total of 57 participants and were presented at a high level in the press release: (i) MARD of 13.9% vs. YSI with seven-day wear (n=15) - Day 1 in-clinic MARD was 13.7%, Day 4 in-clinic MARD was 14.5%, Day 7 in-clinic MARD was 14.8%; (ii) MARD of 13.3% vs. YSI with 10-day wear (n=15); and (iii) a seven-day head-to-head study demonstrating MARD of 11.1% vs. Dexcom G5's MARD of 12.2%. The first and second studies were based on earlier versions of sensor manufacturing process and calibration algorithms, hence the improved accuracy in the third study. WaveForm said that the calibration was "not a retro fit" and "essentially what the user would see." The team added that "the calibration component of the algorithm is applied to the data after the data is downloaded at the end of the study. The only post processing that occurs is calibration." We did not completely understand the answer and look forward to seeing whether this encouraging data is confirmed in a pivotal and real-world setting. There were no reported safety issues in any of the studies. We found it notable the day one performance was actually better, perhaps because of the low-trauma insertion. These studies did not test 14-plus-day wear, but the next one in the second half of February will.

The company says that the sensor algorithm will be improved in early 2018, and the results of the trials support commencement of a European pivotal study to secure a CE mark and launch in 2018. Discussions are ongoing with several sites in the EU for a pivotal study and more details will be provided in the coming months. Clinical trials to support PMA submission could begin "as early as 2019" - the same rep told us that the plan is to obtain an IDE for the US by the end of 3Q18. Ultimately, the current plan is to work with a partner to commercialize the sensor in the EU, but retain commercial rights in the US and Asia.

WaveForm intends to develop a "vertically integrated AP system" - all components in-house, similar to Medtronic - beginning in 2018. At this stage, the company has identified a pump candidate that it "may" elect to use in an initial clinical study, but is still exploring several "pump/insulin delivery options" - the goal is to ultimately own or have a pump built. On the algorithm front, AgaMatrix has evaluated "several," and plans to license one, modifying it in the coming months in advance of the first trials. We are a bit surprised that it wasn't possible for them to purchase Animas, but perhaps they could not meet on price (instead, J&J is writing off the investment).

- **We last covered AgaMatrix/WaveForm in October, when the company secured $32 million loans and announced the CGM plans for a CE Mark in 2018** - read the coverage here.
- **Here are pictures of the CGM (i) provided by the company and (ii) from the DTM poster**; we're not sure if the on-body component will get smaller (its depth, in particular, may be a drawback relative to other options though it's hard at this stage to compare) and believe that will be a crucial area to improve before launch. The app looks fairly intuitive and user-friendly, and the applicator looks very consumer-friendly.



Selected Q&A with WaveForm Technologies

Q: Can you give more details on the studies, especially the Dexcom G5 trial, including: (i) comparator - YSI or BGM?; (ii) prospective calibration for WaveForm? (i.e., this was not a retrofit of the raw sensor signal, but what a patient would see?); and (iii) how often fingerstick calibrations were done?

A: (i) We have conducted four clinical studies in 2017. A total of 57 subjects participated in the studies. One study was conducted in Canada and three were conducted in E.U. Two of the studies were 7-day wear studies and two were 10-day sensor wear studies. The studies were structured following well-established performance assessment protocols.

In the 7 day studies, there were three in-clinic days (days 1, 4 and 7) and in the 10-day studies there were four in-clinic days (days 1, 4, 7 and 10). During the in-clinic days blood was drawn every 15 minutes and two plasma glucose analyses were conducted on each sample using an YSI. The in-clinic day lasted 12 hours and the blood glucose levels were modulated so that at least 10% of the values were >275 mg/dl and <70 mg/dl. The performance analysis was based on the prospective application of our calibration algorithm on the in-clinic data using one YSI calibration value. The MARD and MAD values were determined on each YSI/CGM data pair.

The Dexcom trial was based on a 10-day protocol, similar to the one described above. On day one there were two WaveForm sensors applied to each subject in the abdominal area. Since the Dexcom sensors are only authorized for 7 days of use, the Dexcom sensor was applied to the abdominal area at the beginning of the in-clinic day 4. The comparison between WaveForm and Dexcom was made based upon the first 7 days of use for both the WaveForm (days 1-7) and Dexcom (day 4-10). The Dexcom sensor was calibrated using two YSI values at the beginning of each in-clinic day. The MARD and MAD calculations of Dexcom sensors were made by pairing sensor values with the most coincident YSI reading. All measures of MARD and MAD were calculated as compared to the YSI plasma glucose values.

(ii) The calibration is not a retro fit, it is essentially what the user would see. However, the subject is only able to see the WaveForm CGM current data as it is generated and transmitted to the receiver. The measuring component of algorithm has been incorporated in the firmware of the transmitter but the calibration component of the algorithm is applied to the data after the data is downloaded at the end of the study. The only post processing that occurs is calibration, but it is not a retro fit. The calibration component of the algorithm is applied to the data from each in-clinic day using the first YSI value from that day as the single calibration point. For this analysis, it would be fair to say the WaveForm sensor uses only one calibration point per day while Dexcom sensor benefits from a cumulative set of calibration points over the 7 days.

Our current product development plan, and clinical data to date, suggest that we would recommend one to two "day-1" calibrations for our CGM device (importantly, with only a one hour "warm up" time), then one calibration every day, or potentially every other day.

We do believe a "factory calibrated" or "no calibration" CGM may be feasible - however, given the clinical importance of obtaining the most accurate and consistent glucose score possible, especially as relates to directing insulin therapy, we wouldn't intend to rush to a "no calibration" system just to satisfy a marketing hope, or claim.

(iii) With respect to the in-clinic days, no fingerstick calibrations were done with regards to the WaveForm or Dexcom.

With respect to non-in clinic days, 2 finger sticks were used for Dexcom. The subjects were asked to take a total of 5 BGM readings for each of the non-in clinic days.

Q: Sounds like it's going to be a 14-day sensor, but the studies only tested it out to 7-10 days? Will EU launch be for 10 days or 14 days?

A: We believe the technical and clinical data obtained to date supports a plan to launch our sensor with a 14-day wear life. We will conduct a 14-day study in the second half of February that we believe will confirm the performance of our sensor for 14 days. We believe our proprietary sensor design and polymer may provide flexibility for even longer potential sensor life in the future.

Q: Will AgaMatrix Holdings/WaveForm need to raise additional capital for EU commercialization? For US pivotal commercialization?

We are currently exploring a variety of strategic and financial discussions as relates to the development and commercialization of our CGM and AP product candidates, and given the rapid recent developments and changes in the diabetes technology market, interest in our program from a variety of parties is very high.

We have the capital we need to get to E.U. approval, and look forward to further announcements in the coming months as to our commercial, strategic and capital plans.

Close Concerns' Remaining Questions

Q: Can WaveForm (AgaMatrix) deliver on this feature set? How will ultimately stack up in Europe to Dexcom's G6, Abbott's FreeStyle Libre (and potentially Abbott's next-gen FreeStyle Libre), Medtronic's Guardian Connect, and Senseonics' Eversense?

Q: When will WaveForm commence the CGM pivotal trial, how large will it be, what sites, and what investigators?

Q: How much will AgaMatrix's BGM manufacturing expertise help? What makes WaveForm confident it can push this CGM to market, whereas Bayer could not/decided not to? What can AgaMatrix/WaveForm learn from Abbott and Roche, BGM players that have taken different paths to propelling CGM?

-- by Brian Levine, Adam Brown, and Kelly Close