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Harbinger Health CEO Stephen Hahn On Early Cancer Detection To 'Move The Needle' On Survival

by Marion Webb

Medtech Insight spoke with Stephen Hahn, ex-FDA commissioner and CEO of Harbinger Health, who attended SXSW, about the firm's blood-based cancer test in development.

SXSW is known for attracting celebrities from the worlds of film, music and tech, and this year drew a unique combination of medical, regulatory and entrepreneurial medtech expertise in the person of Stephen Hahn.

Hahn, who led the US Food and Drug Administration through the start of the coronavirus pandemic in 2020 and is now heading up liquid biopsy start-up Harbinger Health, didn't have to travel far to participate in the 13 March panel "*The Science and Politics of Vaccines*", held at the Convention Center in Austin, TX.

Hahn told *Medtech Insight* he moved to Austin two years ago and came to SXSW "to learn, but also participate and contribute" in the event's burgeoning health care and biotech environment. The 2023 conference included a Health & Medtech track covering topics such as femtech, equity, mental health and brain implants.

A longtime oncologist, Hahn was chief medical executive at the University of Texas MD Anderson Cancer Center in Houston prior to joining the FDA in December 2019. He left the agency in January 2021. Five months later, he joined Flagship Pioneering, described by its founder Noubar Afeyan as a "venture-production firm" because it creates and funds all of its own ventures in-house. Its portfolio includes COVID-19 vaccine maker *Moderna, Inc.*, *Tessera Therapeutics*, which focuses on gene writing, and *Generate Biomedicines*, which applies artificial intelligence to designing novel proteins.

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Source: Harbinger Health

Harbinger Health launched in December 2021 with $50m of committed capital from Flagship Pioneering and Hahn at the company's helm.

Harbinger aims to differentiate itself from large competitors in blood-based cancer testing, such as *GRAIL, Inc.*'s Galleri and *Thrive Bioscience Inc.*'s CancerSEEK test (now part of *Exact Sciences Corp.*), on multiple fronts.

"It's the access, cost, positive predictive value, knowing that if the test is positive, it's really positive," Hahn said. "And this early-stage sensitivity that really does distinguish our company."

Hahn hopes to market Harbinger's test for about $150. This compares to Grail's Galleri multi-cancer early detection test, which has a list price of $949. Grail markets Galleri as a laboratory developed test and is currently pursuing FDA approval. Harbinger also wants to make a more accurate test with of 70% or higher positive predictive value (PPV), which would surpass those of Grail and Exact Sciences.

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But Hahn is confident "there is plenty of room for all" in the global liquid biopsy market, which is expected to grow at a compound annual rate of 26.8% from 2020 to $6.1bn by 2025, according to Citeline's *Meddevicetracker report* on the space.

Harbinger is currently conducting a 10,000-participant study with the Sarah Cannon Research Institute to validate and develop its early-cancer test. Hahn expects to announce results in 2024.

In a 14 March interview with *Medtech Insight*, Hahn discussed the future of vaccine development and innovation, Harbinger's AI-enabled technology, opportunities and challenges in the liquid biopsy space, as well as the end of the Public Health Emergency. This article was lightly edited for length and clarity.

Q ***Medtech Insight*: What is the post-pandemic future of vaccine development and innovation?**

A Stephen Hahn: The big takeaways are No. 1, we demonstrated during 2020 into early 2021 that we could really fulfill the promise of accelerating innovation. Never in the history of FDA – and I suspect mankind – was a vaccine developed in that period of time, went through the rigorous testing that it did, and then ultimately authorized – understanding that the standard is different for an EUA than it is for a biological license application, which is approval.

We showed that we could reduce barriers on that effort, work with the private sector, and if we didn't have a robust private sector, we probably wouldn't have gotten done what we got done. If you think about the hundreds of thousands of lives per month that are saved by having a vaccine, that's a pretty remarkable effort. We should be doing that more in the future. There isn't any reason why these great innovations that we're seeing in medicine and health can't be accelerated, understanding that we need from the regulators' point of view appropriate oversight. The other major point is we learned and relearned the lesson that a lot of people in the US [and] around the world are left behind – don't have access to care, products, etc. The private sector with government can help us solve that problem.

Q **How might FDA leverage COVID-19 lessons going forward with respect to in-vitro diagnostics and laboratory-developed tests?**

A Hahn: We learned a lot. I think, after some initial hiccups, we gave a lot of regulatory flexibility. There is a double-edged sword to regulatory flexibility, because sometimes the market can be flooded with tests that don't give the right answer. There needs to be a balance. In the beginning of a pandemic, allowing tests to get on the market that have appropriate oversight, but really understanding that they're not going to be tested to the same degree that they would in normal times, we've got to be okay with that.

And we've got to be able to go back and adjust the test and the decision based upon

real-world evidence that we collect. But I do think for complicated tests – that's where Harbinger Health comes in – we're a complicated set of cancer-based diagnostics, and there needs to be, in a high-risk setting, appropriate oversight. The consequences of clinical decision-making are substantial: Do you have cancer or not? Do you need work-up? Do you need a biopsy? Those are not minor, they're life-altering and potentially life-threatening questions that need to be answered in advance and accurately.

We published in the New England Journal, when I was at the agency in August of 2020, a review of our experience with laboratory-developed tests with COVID. A substantial number, over 50%, had problems that had to be fixed. That's not surprising, right? What it means is let's work together with industry in an emergency and then fix them, but you need the oversight to do that. (Also see "*'All Options On The Table,' Says Hillebrenner On Diagnostics Reform*" - Medtech Insight, 23 Feb, 2023.)

The FDA and some folks in Congress have pushed for the *VALID Act*, which would provide more clarity around the FDA's roles and responsibility. [The Verifying Accurate Leading-Edge IVCT Development Act sought to change the current regulatory scheme for clinical laboratory-developed tests and in-vitro clinical tests] You probably also know that in August of 2020, the Department of Health and Human Services – and I was on the public record being against this – we issued a statement saying that FDA did not have the authority to regulate laboratory developed tests. It's a grey area and one that will be subject to litigation, in my opinion. Where I come down on this is that I think the agency definitely has a role to play in complex, high-risk diagnostic tests.

Q **What attracted you to Flagship Pioneering?**

A Hahn: I joined Flagship Pioneering because of two reasons, firstly their leader Noubar Afeyan and his approach of using biology to form new companies and really to be rooted in the science that was greatly appealing to me.

Secondly, I joined Flagship's Preemptive Medicine and Health Security Initiative. We

have a lot of chronic disease out there that will cause significant symptoms in people, but also could kill people. The question that we're asking is, 'What if we could identify these diseases before they manifest themselves?' The apparent one is cancer, because if you diagnose cancer early, you have a better chance of surviving and the treatments are less toxic. If we can use science, company formation, to solve these problems, like we did with respect to vaccines and COVID, that's a real win for everybody around the world.

Q **Can you explain the science behind Harbinger's technology?**

A Hahn: The biological basis of this company is a signature we can detect in someone's genes that there is the possibility of cancer being present. There is a lot of evidence to suggest that cancer starts significantly before you see it on a scan and significantly before you're diagnosed. Many of the common cancers that we face are cancers that are diagnosed in patients that are advanced and often incurable. Our biological signature, which is initially found in tissue, but now we can detect it in blood, allows us to detect it at a very early stage, robustly. And if we're going to make a difference in the world, it's going to be diagnosing stage one or stage two disease.

Q **What makes Harbinger's test different from existing blood tests for early detection of cancer?**

A Hahn: We also focus on access, which has two components. It's got to be affordable, something like a cholesterol test or other tests you routinely get. It has to be clinically informative. One of the problems with the current set of tests is something called PPV, positive predictive value, which is how doctors practice. When I order a test, like a COVID test, I want to know in this patient population, is there a high chance that when it's positive, it actually means a positive? And you can imagine what that means in cancer, right? It's a deficit right now, this positive predictive value issue. (Also see "*HLTH 2022 Roundup: Mirvie, Grail, Biofourmis, Komodo Health, Babson Diagnostics*" - Medtech Insight, 17 Nov, 2022.)

We're looking to push that positive predictive value to a number 70% or greater.

That's our development plan that allows the most clinical informativeness for physicians. We're aiming for a price point of $150 or less for the initial screen. I'd love for it to be even lower, and the technology's just got to get there. But our biology allows us to even entertain that. And I am sure that others in the field are thinking the same thing, and they should, and there's plenty of room for all of us. (Also see "*Liquid Biopsy Revolutionizing Cancer Care, But Costs Continue To Inhibit Global Potential*" - Medtech Insight, 29 Sep, 2022.)

Q **Can you talk about the Cancer ORigin Epigenetics-Harbinger Health (CORE-HH) 10,000-participant study. What types of cancer and how many types of cancer are being evaluated in this study?**

A Hahn: We have what's called a pan-cancer test. Notice I'm not saying universal and I'm being deliberate about that, because we don't know the answer to that question. Our current CORE-HH study is designed to look at 20 cancers and 20 of the most common cancers that afflict folks around the world.

We'll also determine whether in some of the other less common cancers we see this signature. That's our base case and where we're starting with respect to this. Because this is a signature that appears to be linked to the development of cancer early on, we see it in quite a few cancers. It could be that we determine that the best use cases are single cancers or a group of cancers, and we're maintaining that optionality to add the absolute best impact for cancer patients.

Q **Are you looking for a single signature to detect multiple cancers or multiple signatures?**

A Hahn: There is a pan-cancer signature that appears to be present in our pilot data in a number of cancers, 19 to 20, and it is what we're pursuing in our CORE-HH trial (a case control study). But we also have in our discovery processes determined there are other additional components to a signature that allows us to sort of figure out, Is it lung? Is it breast? Is it colon? So, there's additional information from a person's genome that can help us figure out some of these things.

> We also realize that diversity is going to be very, very, very important in what we're doing, and that's not to suggest that this is entertaining a conversation about genetic diversity other than we know that families have different components to their genome, which affect who they are and what they're about biologically, and there's no reason to think that that's not true with cancer. And we have to sort that out and use that information as best as possible to make the best judgment and recommendation for physicians, providers, patients, consumers.

Q How far in advance do you hope Harbinger's test will be able to detect cancer?

A Hahn: Right now we're focused on diagnosing stage one and two before someone has symptoms at stage three and four. But we believe that that this could be pushed to an even earlier time point. We believe that there isn't any reason that sometime in the next 5, 10, 15 years, diagnoses can be made in the blood as opposed to biopsy. Right now, blood leads you in a certain direction, you need to do a biopsy. That's the right thing to do.

Q What are the criteria for study participants?

A Hahn: We've employed what we think is a pretty common definition. We know that cancer is a disease of getting older – 50% of American men develop a cancer, between 30 and 40% of women develop a cancer – so it's a pretty significant issue as people age. Right now, the criteria are between the age of 45-75. It's kind of an aggregate of the general population who aren't necessarily high risk by definition, but who just would come to the doctor for their normal sort of checkup, etc. We also imagine a world where we start screening kids, because kids get cancers too, and they're very curable. We're not there yet and we're not going there right now. (Also see "*FDA Draft Guidance Takes Aim At Racial, Ethnic Disparities In Clinical Trials*" - Medtech Insight, 13 Apr, 2022.)

Q When will first results be made available from the study?

A Hahn: We're looking to complete this study this year, and we'll have answers to the

study in 2024. We're using artificial intelligence and machine learning to help us refine our algorithms. It's interesting in this work, there's the potential as you do this for a lot of biases. The biases could be gender, ethnicity, race, age, other diseases, etc. We have to be really careful that we have enough representation of these variables to actually figure that out. We want not only clinical informativeness, but we realize that every tube of blood represents a human being and their family who are entrusting us with a question, 'Do I have cancer?' We have to be very, very sure of the quality of that answer.

Q **It's early, but how will the study results help advance your product development strategy?**

A Hahn: Our study is broad. It also has an adaptive design, which allows us to add or subtract folks based upon the variables that I just described that would affect it. It will give us the opportunity to ask the question, What should our product look like? Should it be a 20 cancer-pan test, a group of cancers, a single test like pancreatic cancer? It'll be a data-driven decision from this trial.

Q **What is your hope for the Cancer Moonshot Initiative?**

A Hahn: I'm glad to see there is a renewed effort into that and kudos to the Administration for pushing that forward. I think a big part of that is in fact screening and early identification of cancer. If you think about where we are with cancer right now, and let's take a disease like pancreatic cancer, which is a really difficult disease – 95% of folks are diagnosed with advanced disease, 5% five-year survival. If you could diagnose even 50% of folks with pancreatic cancer at stage one and two disease, one would hypothesize that you can really move the needle in terms of people surviving, and it would open up new areas of potential therapies. I think one of the big ways that the Cancer Moonshot, I have a bias admittedly, could move the needle with respect to reduction in mortality is the early identification of cancers. Focus on diversity is also important. Something that I learned in the pandemic and was really important to me is that we're leaving too many people behind. (Also see "*Biden Shouts Out 'Cancer Moonshot' In State Of The Union*" - Medtech Insight, 8 Feb, 2023.)

Q **Is your company going to get involved in this initiative?**

A Hahn: I think we want to complete our CORE-HH trial to see where we are from a data point of view, but we'd be very anxious to participate in an effort such as this around the country and the world to reduce the morbidity and mortality associated with cancer. So yeah, we'd be very interested.

Q **The COVID-19 Public Health Emergency is set to end in May. What should the industry be watching for during that transition especially as it relates to emergency use authorization?**

A Hahn: I think we're seeing the agency speak to what does that off-ramp look like, because as you know, after the recission of a public health emergency, there won't be any issuance of EUAs anymore, but the agency as far as I can tell from the language in the draft guidances, is committed to providing an off-ramp from EUA to outright approval. Companies should really be having those conversations now with the relative divisions of the FDA. (Also see "*So The Public Health Emergency Is Over. Now What?*" - Medtech Insight, 28 Feb, 2023.)

'What are you going to need to see from us to actually make that transition?' Now there may be some instances where companies don't want to fill out right approval, but I suspect many will. (Also see "*Top 100 Outlook 2021: Medtechs Look To Build On Experiences Of Serving Global Markets In A Pandemic*" - Medtech Insight, 4 Dec, 2020.)

Hopefully the companies have done what the diagnostic companies did early, which is collect real-world data after an emergency use authorization, collect those data, see how your performance is. I'm very confident that the FDA will want to see those data as part of this transition.