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BUSINESS

Hot Startup Theranos Has Struggled With Its Blood-Test Technology

Silicon Valley lab, led by Elizabeth Holmes, is valued at \$9 billion but isn't using its technology for all the tests it offers

By John Carreyrou

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On Theranos Inc.'s website, company founder Elizabeth Holmes holds up a tiny vial to show how the startup's "breakthrough advancements have made it possible to quickly process the full range of laboratory tests from a few drops of blood."

The company offers more than 240 tests, ranging from cholesterol to cancer. It claims its technology can work with just a finger prick. Investors have poured more than \$400 million into Theranos, valuing it at \$9 billion and her majority stake at more than half that. The 31-year-old Ms. Holmes's bold talk and black turtlenecks draw comparisons to Apple Inc. cofounder Steve Jobs.

But Theranos has struggled behind the scenes to turn the excitement over its technology into reality. At the end of 2014, the lab instrument developed as the linchpin of its strategy handled just a small fraction of the tests then sold to consumers, according to four former employees.

One former senior employee says Theranos was routinely using the device, named Edison after the prolific inventor, for only 15 tests in December 2014. Some employees were leery about the machine's accuracy, according to the former employees and emails reviewed by The Wall Street Journal.

In a complaint to regulators, one Theranos employee accused the company of failing to report test results that raised questions about the precision of the Edison system. Such a failure could be a violation of federal rules for laboratories, the former employee said.

Theranos also hasn't disclosed publicly that it does the vast majority of its tests with traditional machines bought from companies like Siemens AG.

The Palo Alto, Calif., company says it abides by all applicable federal lab regulations and hasn't exaggerated its achievements. It disputes that its device could do just 15 tests, declining to say how many tests it now handles or to respond to some questions about its lab procedures, citing "trade secrets."

But Theranos's outside lawyer, David Boies, acknowledges that the company isn't yet using the device for all the tests Theranos offers. The transition to doing every test with the device is "a journey," he says.

DEVELOPING

- Theranos Dials Back Lab Tests at FDA's Behest

Asked about the claim on the company's website, Mr. Boies replied that using the device for the "full range" of blood tests is a goal Theranos will eventually achieve.

Theranos points out that it has publicly disclosed doing "certain esoteric and less commonly ordered tests" with traditional machines on blood drawn with smaller needles from veins.

During the Journal's reporting, Theranos deleted a sentence on its website that said: "Many of our tests require only a few drops of blood." It also dropped a reference to collecting "usually

only three tiny micro-vials” per sample, “instead of the usual six or more large ones.” Heather King, the company’s general counsel, says the changes were made for “marketing accuracy.”

Ms. King and Mr. Boies say Theranos’s lab work is accurate. Theranos has performed tests on millions of patients referred by thousands of doctors and has received highly positive feedback, they say.

Ms. Holmes, Theranos’s chairman and chief executive, declined interview requests from the Journal for more than five months. Last week, the company said she would be available to comment, but her schedule didn’t allow it before publication of this article.

User-friendliness

Some doctors appreciate the company’s user-friendliness. Results sometimes arrive within 15 minutes, says Scott Wood, a primary-care doctor in Menlo Park, Calif. “That’s exciting and could be very useful in emergency situations,” he says. When patients ask about trying Theranos, he replies: “Sure, go ahead.”

Other doctors said they stopped steering patients to Theranos because of results they didn’t trust. “I don’t want my patients going there until more information and a better protocol are in place,” says Gary Betz, an internist in Phoenix.

Ms. Holmes launched Theranos in 2003 when she was 19 and dropped out of Stanford University in her sophomore year.

Theranos is built around Ms. Holmes’s self-professed phobia of needles. She has said in numerous public appearances that drawing a tiny amount of blood at a time from each patient’s finger and avoiding the large syringes used by traditional labs will make patients less reluctant to get blood tests. That will lead to earlier diagnoses and save lives, according to Ms. Holmes.

Her first idea was a small arm patch to screen blood for infectious diseases and deliver antibiotics, according to Phyllis Gardner, a Stanford medical-school professor with whom Ms. Holmes consulted at the time. The patch never made it to market.

“She was a young kid with only rudimentary engineering training and no medical training,” says Dr. Gardner, whose husband was a member of a Theranos advisory board and still owns shares in the company.

In 2005, Ms. Holmes hired Ian Gibbons, a British biochemist who had researched systems to handle and process tiny quantities of fluids. His collaboration with other Theranos scientists produced 23 patents, according to records filed with the U.S. Patent and Trademark Office. Ms. Holmes is listed as a co-inventor on 19 of the patents.

The patents show how Ms. Holmes’s original idea morphed into the company’s business model. But progress was slow. Dr. Gibbons “told me nothing was working,” says his widow, Rochelle.

In May 2013, Dr. Gibbons committed suicide. Theranos’s Ms. King says the scientist “was frequently absent from work in the last years of his life, due to health and other problems.” Theranos disputes the claim that its technology was failing.

After Dr. Gibbons’s widow spoke to a Journal reporter, a lawyer representing Theranos sent her a letter threatening to sue her if she continued to make “false statements” about Ms. Holmes and disclose confidential information. Ms. Gibbons owns Theranos shares that she inherited from her husband.

Two giant rivals

Theranos began offering tests to the public in late 2013. It opened 42 blood-drawing “wellness centers” in the Phoenix area, two in California and one in Pennsylvania. Most are in Walgreens Boots Alliance Inc. drugstores.

Ms. Holmes successfully lobbied for an Arizona law that allows people to get tests without a doctor’s order. Theranos’s promise of fast results and prices that are “a fraction” of other labs pits it against Quest Diagnostics Inc. and Laboratory Corp. of America Holdings, which dominate the \$75 billion-a-year blood-testing industry in the U.S.

While the biggest venture-capital firms specializing in health care aren’t listed as Theranos investors, Oracle Corp. cofounder Larry Ellison and venture-capital firm Draper Fisher Jurvetson, have bought stakes in Theranos, according to data from Dow Jones VentureSource.

Theranos has raised several rounds of financing, most recently in June 2014. Like most closely held companies, Theranos has divulged little about its operations or financial results.



A 'nanotainer' developed by Theranos to help it run tests from just a few drops of blood pricked from a person's finger. The tiny tube is about half an inch long. PHOTO: MARTIN E. KLIMEK

Clinical labs usually buy their testing instruments from diagnostic equipment makers. Before those makers can sell to labs, they must undergo vetting by the Food and Drug Administration.

Because Theranos doesn't sell its Edison machines to other labs, it didn't need the FDA's approval to start selling its tests. Still, the company has sought clearance for more than 120 of its tests in an effort to be rigorous and transparent.

In July, Theranos announced the first FDA clearance of one of those tests, which detects herpes. The FDA and Theranos decline to comment on the status of the other submissions.

Whether labs buy their testing instruments or develop them internally, all are required to prove to the federal Centers for Medicare and Medicaid Services that they can produce accurate results. The process is known as proficiency testing and is administered by accredited organizations that send samples to labs several times a year.

Labs must test those samples and report back the results, which aren't disclosed to the public. If a lab's results are close to the average of those in a peer group, the lab receives a passing grade.

In early 2014, Theranos split some of the proficiency-testing samples it got into two pieces, according to internal emails reviewed by the Journal. One was tested with Edison machines and the other with instruments from other companies.

The two types of equipment gave different results when testing for vitamin D, two thyroid hormones and prostate cancer. The gap suggested to some employees that the Edison results were off, according to the internal emails and people familiar with the findings.

Senior lab employees showed both sets of results to Sunny Balwani, Theranos's president and chief operating officer. In an email, one employee said he had read "through the regulations more finely" and asked which results should be reported back to the test administrators and government.

Mr. Balwani replied the next day, copying in Ms. Holmes. "I am extremely irritated and frustrated by folks with no legal background taking legal positions and interpretations on these matters," he wrote. "This must stop."

He added that the "samples should have never run on Edisons to begin with."

Former employees say Mr. Balwani ordered lab personnel to stop using Edison machines on any of the proficiency-testing samples and report only the results from instruments bought from other companies.

The former employees say they did what they were told but were concerned that the instructions violated federal rules, which state that a lab must handle "proficiency testing

samples...in the same manner as it tests patient specimens” and by “using the laboratory’s routine methods.”

In its everyday business at the time, Theranos routinely used Edison machines to test patients’ blood samples for vitamin D, the two thyroid hormones and prostate cancer, the former employees say.

In March 2014, a Theranos employee using the alias Colin Ramirez alleged to New York state’s public-health lab that the company might have manipulated the proficiency-testing process.

Stephanie Shulman, director of the public-health lab’s clinical-lab evaluation program, responded that the practices described by the anonymous employee would be a “violation of the state and federal requirements,” according to a copy of her email.

What the employee described sounded like “a form of PT cheating,” Ms. Shulman added, using an abbreviation for proficiency testing. She referred the Theranos employee to the public-health lab’s investigations unit.

The New York State Department of Health confirms that it got a formal complaint in April 2014 “in regard to testing practices at Theranos” and forwarded it to the Centers for Medicare and Medicaid Services.

Asked about the complaint, Theranos confirms that the Edison system produced results for several tests last year that differed from results obtained from traditional equipment.

Leftover samples

But that comparison was based on “left-over proficiency testing samples” used “to conduct additional experiments and verify best practices,” says Ms. King, Theranos’s general counsel. The company has never failed proficiency testing, she adds.

She says Mr. Balwani’s instructions were consistent with the company’s “alternative assessment procedures,” which it adopted because it believes its unique technology has no peer group and can be thrown off by the preservatives used in proficiency-testing samples.

Theranos has been “upfront and transparent with regulators” about the procedures, Ms. King adds.

As of the end of 2014, Theranos did less than 10% of its tests on Edison machines, including tests for prostate cancer and pregnancy, one former senior employee says.

In addition to the 15 tests run on the Edison system, Theranos did about 60 more on traditional machines using a special dilution method, the former senior employee says. The company often collected such a small amount of blood that it had to increase those samples’ volume to specifications required by those traditional machines, former employees say.

A third set of about 130 tests was run on traditional machines using larger samples drawn from patients’ arms with a needle.

For tests done with dilution, the process caused the concentration of substances in the blood being measured to fall below the machines’ approved range, three former employees say. Lab experts say the practice could increase the chance of erroneous results.

Most labs dilute samples only in narrow circumstances, such as when trying to find out by how much a patient has overdosed on a drug, say lab experts.

“Anytime you dilute a sample, you’re adulterating the sample and changing it in some fashion, and that introduces more potential for error,” says Timothy R. Hamill, vice chairman of the University of California, San Francisco’s department of laboratory medicine. Using dilution frequently is “poor laboratory practice.”

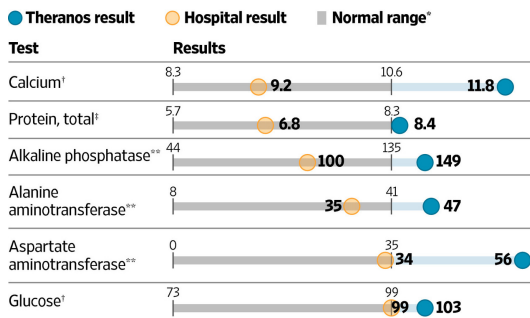
Theranos says dilution is common in labs but declines to say if it dilutes samples. Theranos’s “methods for preparing samples for analysis are trade secrets and cannot be revealed,” Ms. King says.

Those methods “have been disclosed” to regulators and don’t “adversely impact the quality of its tests or the accuracy of its test results,” she adds.

Former employees say diluting blood drawn from fingers contributed to accuracy problems early last year with a test to measure potassium. Lab experts say finger-pricked blood samples

Same Patient, Different Results

For one Arizona woman, Theranos found abnormally high levels for six tests. Hospital tests two days later were normal. Theranos says variation across labs is commonplace and can be caused by medicines and diet.



*As stated by Theranos †in milligrams per deciliter ‡in grams per deciliter

**liver enzyme test, in units per liter

Sources: Theranos and HonorHealth Scottsdale Shea Medical Center via Nicole Sundene and Maureen Glunz
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can be less pure than those drawn from a vein because finger-pricked blood often mixes with fluids from tissue and cells that can interfere with tests.

Some of the potassium results at Theranos were so high that patients would have to be dead for the results to be correct, according to one former employee.

Ms. King denies any problems with the potassium test and says Theranos has no indication that “inaccurate results were returned to patients.”

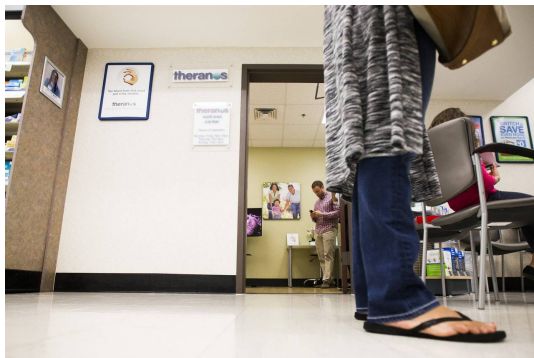
Theranos challenged interpretations of its test results by health-care providers and patients whose medical records were reviewed by the Journal.

After those people spoke to the Journal, Theranos visited some of them and asked them to sign prepared statements that said the Journal mischaracterized their comments. Two did and one refused.

Carmen Washington, a nurse who worked at a clinic owned by Walgreens in Phoenix, says she began to question Theranos’s accuracy after seeing abnormal results in potassium and thyroid tests.

She says she raised her concerns with the drugstore operator and Theranos’s lab director, asking for data to show that the company’s finger-prick testing procedures produced results as accurate as blood drawn from a vein.

“They were never able to produce them,” she says. Ms. King says the company did show detailed testing-accuracy data to the nurse.



Theranos began offering testing to the public in late 2013. It opened 42 blood-drawing sites that it calls ‘wellness centers’ in the Phoenix area, two in California and one in Pennsylvania. Most are in Walgreens stores, including this one in Scottsdale, Ariz.

PHOTO: MICHAEL CHOW/THE ARIZONA REPUBLIC

A Walgreens spokesman says the nurse kept writing lab orders for Theranos tests until she stopped working at the clinic in February. Walgreens says its partnership with Theranos has gone smoothly overall.

About a dozen doctors and nurses complained about test results by phone or email to the company from late 2013 to late 2014, a person familiar with the matter says. The Arizona attorney general’s office, state health department and Better Business Bureau say they have received no complaints about Theranos.

A second opinion

Dr. Betz, the Phoenix doctor, says one of his female patients went to Theranos in August 2014 for a routine potassium test to monitor potential side effects from her blood-pressure

medication. He says Theranos reported that her potassium level was close to the threshold considered critical.

Another lab reran the test three days later. The results came back normal.

Ms. King says Dr. Betz's nurses kept sending patients to Theranos until early this year.

Real-estate agent Maureen Glunz went to Theranos a few days before last Thanksgiving after complaining of ringing in her ear. Her blood was drawn from a vein in her arm. The results showed abnormally elevated levels of glucose, calcium, total protein and three liver enzymes.

Her primary-care doctor, Nicole Sundene, who is a naturopath, worried that Ms. Glunz might be at risk of a stroke and asked her to go to an emergency room. The hospital's tests two days later showed nothing abnormal.

Dr. Hamill of UC San Francisco says some of Ms. Glunz's results should "have fairly steady values...over relatively long time periods."

Ms. King says "some degree of variability in lab results across different laboratories is commonplace," adding that Ms. Glunz's medication and diet could have caused "fluctuations" in her results. None of the results were "close to the critical range," Ms. King adds.

It is misleading to draw conclusions from "a handful of patient anecdotes," she says.

Ms. Glunz says she likes Theranos's low prices and would go there again if she could be sure its tests are accurate. "But trial and error on people, that's not OK," she says.

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