Opinion Paper

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The meteoric rise and dramatic fall of Theranos: lessons learned for the diagnostic industry

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Abstract: In this piece we discuss and reflect on the conclusion of the Theranos saga in the light of its fraud conviction. Theranos (founded in 2003 by Elizabeth Holmes) was supposed to disrupt the diagnostic testing industry by developing technology which could perform dozens of tests using a tiny amount of blood from a finger-prick. As a result, Ms. Holmes rose to fame, becoming the world's youngest female self-made billionaire and was plastered across magazine covers. However, in 2014, Theranos began to fall apart following increasingly damaging revelations regarding its lack of expertise, technology, framework, extreme secrecy and inaccurate test results. This led to the closure of two of its laboratories, investor and patient lawsuits and the devaluation of Ms. Holmes's wealth to nothing. In March 2018, the United States Security Exchange Commission ordered Ms. Holmes to pay \$500,000 to settle the charge of massive fraud and barred her from being a director of a publicly owned company for 10 years, likely concluding Theranos's endeavors. We conclude our series of articles on this topic by reflecting on the lessons the laboratory medicine community can learn from Theranos.

Keywords: genomics; mass spectrometry; proteomics; translational research.

Introduction

The biotechnology company Theranos was founded by then 19-year-old Stanford dropout Elizabeth Holmes in 2003 with a promise to revolutionize blood testing and diagnostics. Theranos's technology diverged dramatically from the established laboratory medicine paradigm: its tests would use a miniscule amount of blood collected by finger prick instead of traditional venipuncture. This tiny sample would be analyzed by dozens of different panels in Theranos's "Edison Machines", undergoing tests from cholesterol to cancer [1].

Not only did Theranos advocate for a new testing method, it aimed to create a system where patients could select, order and analyze their own tests without clinician oversight. Thus, Ms. Holmes claimed to be 'democratizing' medicine and empowering patients, but also even detecting health problems earlier by improving access to testing. Theranos promised to charge Medicare/Medicaid less than half the rates charged by conventional providers and was projected to save the US government millions of dollars in the next decade [2].

Public response

Theranos and its young, charismatic founder (who has a fear of needles) received near universal acclaim. Theranos's innovative framework to make blood testing timely, simple, cheap and painless resonated in Silicon Valley and around the world. Images of Ms. Holmes posing with a microtube of blood were emblazoned across media outlets and magazine covers and she was hailed as the next Steve Jobs [1–3].

Elizabeth Holmes recruited several industry and political giants to Theranos's advisory board including former US cabinet secretaries, senators and military figures. By 2014, she had accrued \$900 million in funding and Theranos was valued at \$9 billion [3]. Forbes listed her wealth at \$4.5 billion and Ms. Holmes became the world's youngest (self-made) female billionaire at age 30 [4].

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In 2013, Walgreens (an American pharmacy giant) signed a deal to install Theranos Wellness Centers in dozens of its stores. Theranos also partnered with the Cleveland Clinic and Capital BlueCross (a large American health insurance provider) in July 2015 [1].

Emerging problems

Despite all the excitement, in late 2015, news outlets (notably the *Wall Street Journal*) began to voice concerns about Theranos's secrecy and lack of external validation [5]. No specifics or data from the Edison Machine technology were submitted to scientific journals nor made publicly available which was highly unusual for a medical company offering services to members of the public [6]. Thus, no data was available to evaluate the new tests for sensitivity, specificity or robustness nor compare Theranos's products to existing tests. This led to worries about the accuracy of results and patient safety. Two important commentaries labeled Theranos as "stealth medicine", where products, profit and trade secrets were purported to be more important than communicating the knowledge in a peer reviewed scientific forum [7, 8].

In the Laboratory Medicine community, concerns continued to grow about Theranos's exaggerated claims. One of us (EPD) wrote in depth about this in 2015, emphasizing concerns about robustness, sensitivity and specificity [9].

Theranos claimed that results would be electronically delivered in 4 h. However, this did not necessarily give Theranos an advantage over conventional tests. In our institution, the clinical laboratory reports 97% of creatinine and troponin tests in less than 2 h and more than half in 60 min. Moreover, many tests that have a longer turnaround time (such as serum electrophoresis) do not have an immediate impact on patient management so expediting them would not change clinical decisions.

Theranos also wished to disrupt the laboratory medicine paradigm by allowing individuals to order their own blood tests in pharmacy settings. Having patients monitor their own tests without clinician oversight can be dangerous for many reasons [10–13]. Most members of the public are unaware of the complexities of laboratory tests and how to interpret fluctuations in the results. For example, a high prostate specific antigen (PSA) concentration does not always indicate cancer, it could also be a sign of prostatitis or prostatic hyperplasia, which are very common, benign and treatable urologic diseases [9]. False positives from the unproven Theranos tests could cause significant emotional distress including anxiety and depression and

may require unnecessary and costly additional testing to resolve. A patient may be reassured by a false negative result if the test fails to detect signs of disease [10–14].

Physicians should interpret and explain their patients' blood test results within the context of their medical history and environment. For example, higher levels of total protein are normal for some people, and higher levels of CEA may be due to smoking. Clinicians are also more attuned to the variations in test results and what tests are useful for particular patients given their age and condition [15]. The "Choosing Wisely" movement, which is gaining traction, encourages clinicians to carefully select the tests their patients undergo; just because an assay is available does not mean it is needed [16].

Theranos and the American Association for Clinical Chemistry

In 2016, the American Association for Clinical Chemistry (AACC) offered Ms. Holmes a plenary lecture and panel discussion to explain her company's views amid the concerns. It would finally give Clinical Chemists the chance to get answers from this extremely secretive company [17].

Ms. Holmes avoided discussing the company's past, instead focusing on Theranos's transition into a compact instrument company. She introduced the MiniLab: a compact device housing a miniature spectrophotometer, luminometer, cytometer, thermocycler and centrifuge [17].

It is important to note that this prototype represented an engineering, not a biochemical challenge. No breakthroughs or new technologies were presented during the talk nor was the MiniLab subject to external validation [18, 19].

Theranos collapses

By the end of 2015, Theranos had begun to implode. Whistleblowing employees reported that most of the tests Theranos did process were inaccurate or performed on commercially available machines, using normal volumes of blood [6].

Food and Drug Association (FDA) reports from 2014 and 2015 flagged Theranos's tests and facilities. In response, Theranos voluntarily suspended all its tests except for their herpes simplex virus (it is the only FDA-approved offering). Nevertheless, Theranos began to face a string of investigations and allegations from medical

regulators, customers, partners, state legal departments and investors [20].

In March 2016, the *Journal of Clinical Investigation* published the first third-party analysis of Theranos's technology. Their investigation revealed that Theranos tests were outside the normal range almost two times more frequently than standard tests. The authors concluded that the disparities between Theranos's tests and standard tests could harm patients. This was the only independent study ever performed to assess Theranos's claims [21].

After escalating accusations, the Centers for Medicare and Medicaid Services (the American blood testing laboratory overseers) revoked Theranos's license in July 2016. In October 2016 the company laid off 40% of staff and closed its laboratory operations. Theranos also voided 2 years of results from its Edison devices [20].

In 2017, Theranos and Ms. Holmes settled lawsuits from Walgreens, trust funds and the state of Arizona. Forbes now lists Ms. Holmes' wealth at \$0 [20].

In March 2018, the Securities and Exchange Commission (SEC), a major American financial regulator, announced Ms. Holmes would pay a fine of \$500,000 to settle charges of massive fraud (she raised more than \$700 million fraudulently). She is barred from being an officer or director of a publicly owned company for 10 years and gave up control of Theranos. She does not admit any wrong doing [22].

While Theranos continues to work on its Mini Lab technology, it is almost insolvent, and its reputation is in tatters [23]. A book that chronicles Theranos's rise and fall, entitled *Bad Blood: Secrets and Lies in a Silicon Valley Startup* written by *Wall Street Journal* contributor John Carreyrou will be released in May 2018 [24]. A movie will likely follow, starring Jennifer Lawrence and directed by Adam McKay [25].

Conclusions and lessons learned

The Theranos saga contains important lessons for Clinical Chemistry, particularly for individuals and organizations who wish to develop a technology with medical applications. The lessons are summarized in Table 1. We highlight the importance of transparency and the unacceptability of fraud and false claims. Technologies that do not work are bound to fail, regardless of marketing strategies. Indeed, misleading investors, regulators and the public will return to haunt you. It is important to think ahead: hire knowledgeable advisors at the beginning, not when problems arise. Finally, as per the SEC report, it is

Table 1: Lessons learned from Theranos.

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- Be transparent and release peer reviewed data to the scientific community, general public and regulators
 - Do not make false claims about products and be clear about what your product can and cannot do
 - No amount of marketing can make up for technologies that do not work
 - Misleading investors, consumers and regulators will come back to bite you
 - Be proactive: hire knowledgeable advisors right at the beginning, not when problems arise
 - Be clear what your technology can do today – not what you hope it can do someday
 - For AACC, be fair to all vendors, never circumvent the AMOC Committee for presentations at the annual meeting and avoid even perceived conflict of interest
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important to state what your technology can do today, not just what you hope it can do in the future.

This article concludes our series of papers in this journal on the Theranos phenomenon. Could Theranos rise from its ashes? We seriously doubt it.

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